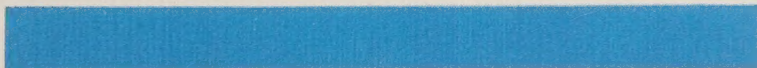


OXYGEN-17 SPIN RELAXATION AND MOLECULAR DYNAMICS IN AQUEOUS SYSTEMS

Bertil Halle



Lund 1981



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IN AQUEOUS SYSTEMS

BERTIL HALLE

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OXYGEN-17 SPIN RELAXATION AND MOLECULAR DYNAMICS IN AQUEOUS SYSTEMS

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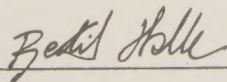
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Abstract Multiexponential spin relaxation, which is of importance for nuclei such as O-17, Mg-25, and Ca-43, was treated by perturbation theory and simple analytical equations for relaxation rates obtained. Relaxation theory for water nuclei in heterogeneous systems, isotropic as well as anisotropic, was developed based on local anisotropy and time-scale separation of water motions. A new interpretation of multinuclear ratios of line splittings was suggested. Oxygen-17 nuclear magnetic resonance (NMR) was used to study water structure and dynamics in aqueous solutions of surfactant micelles, linear polyelectrolytes, and globular proteins. Hydration water is considered as dynamically bound with a lifetime on the order of 10 nanoseconds, while the slightly anisotropic water reorientation is 3 orders of magnitude faster. Charged surface groups produce the largest perturbations. Water penetration into micelles was shown to be slight and head-group and counterion effects were studied. A new method for measuring bound water lifetimes was presented and applied to polyacids. Models for the mechanism of prototropic charge transport in water were formulated and tested against new O-17 scalar relaxation data from normal and heavy water. The relevant NMR theory was developed. A comparison of NMR and conductivity data showed that concerted proton transfer occurs, but only in short chains. Prototropic ions have lifetimes on the order of picoseconds and are prehydrated, i.e. migrate to energetic sinks.			
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Date September 8, 1981

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LIST OF PAPERS

The present thesis consists of this summary and the following papers.

I. NEARLY EXPONENTIAL QUADRUPOLEAR RELAXATION. A PERTURBATION TREATMENT.

B. Halle and H. Wennerström

J. Magn. Reson. 44, 89-100 (1981).

II. INTERPRETATION OF MAGNETIC RESONANCE DATA FROM WATER NUCLEI IN HETEROGENEOUS SYSTEMS.

B. Halle and H. Wennerström

J. Chem. Phys. 75, 1928-1943 (1981).

III. HYDRATION OF IONIC SURFACTANT MICELLES FROM WATER OXYGEN-17 MAGNETIC RELAXATION.

B. Halle and G. Carlström

J. Phys. Chem. 85, 2142-2147 (1981).

IV. WATER OXYGEN-17 MAGNETIC RELAXATION IN POLYELECTROLYTE SOLUTIONS.

B. Halle and L. Piculell

J. Chem. Soc., Faraday Trans. 1, in press.

V. PROTEIN HYDRATION FROM WATER OXYGEN-17 MAGNETIC RELAXATION.

B. Halle, T. Andersson, S. Forsén, and B. Lindman

J. Am. Chem. Soc. 103, 500-508 (1981).

VI. PROTOTROPIC CHARGE TRANSPORT IN WATER.

B. Halle and G. Karlström

Submitted for publication.

And the Lamas go in procession to the lakes and rivers, and partake in this practice. They cast in offerings to the water-nymphs and dragon-spirits of the water, and draw and drink the life-giving and sin-cleansing water, attended by much festivity. Tents are erected in the neighbourhood for about two weeks, during which the multitude drink and bathe in the water, dance, sing, masquerade, and give vent to their joy, in what may be considered a cleansing or atonement feast, as well as a thanks-giving. And monastic discipline even is relaxed during this festival, and many monks are allowed to go home on leave.

1. INTRODUCTION

That water pervades our environment and that it is intimately connected with life must have been recognized already by pre-historic man. Accordingly, water has come to play a prominent part in the creation myths and natural philosophies of virtually every known culture. In the history of human thought, as recorded in the Occident, the first metaphysical system incorporating water as a fundamental element is usually attributed to the Greek philosophers — Thales of Miletos (ca 600 B.C.) in particular. In China, however, water had this status 5300 years ago, when Fû-hsî devised the famous eight trigrams, two of which symbolize water. (One of them is shown on the cover.) Similar attitudes to water can be found in the Upanishads and in Tibetan Buddhist tradition¹ (facing page).

Although deprived of its elemental status through the epoch-making work of Cavendish and Lavoisier in the 1780's, water has continued to hold the fascination of scientist and layman alike. As the remarkable properties of this ubiquitous liquid have been uncovered one by one — from the density maximum studied in the 15th century by members of the Florentine Academy to the hydrophobic interaction, now recognized as a major factor in the structural organization of living systems — water has consolidated its scientific reputation as an eccentric among liquids. Whereas the isolated water molecule is by now characterized in greater detail than any other comparable molecule, we are still a long way from a full understanding of water as a liquid. In fact, the current view of the structure of water is merely a slightly elaborated version of the picture presented half a century ago in the classic work of Bernal and Fowler².

During the past 3500 million years or so, water has played a decisive role in directing the course of biological evolution on

our planet. Indeed, it is hard for our minds — which, incidentally, are 78 percent water — to imagine that life could ever be created and maintained in the absence of liquid water. It is amusing to note how deeply the concept of tetrahedral symmetry permeates our scientific perception of life. Thus, not only does the carbon atom, which forms the backbone of all biomolecules, display tetrahedral covalency, but also water molecules manifest a universal tendency toward local tetrahedral coordination in condensed phases. We know of few chemical facts with more far-reaching consequences. Perhaps we owe an apology to Plato for his much ridiculed speculations in the *Timaios*.

If we are ever to appreciate in depth the subtle molecular drama — with water as one of the main actors as well as the stage — which takes place in living organisms, we must first acquire a thorough knowledge about model systems of increasing complexity. It has been in the hope of contributing towards the attainment of this latter goal, that I have undertaken the work presented here.

2. INTERACTIONS, DYNAMICS AND THE HYDRATION CONCEPT

The phenomenological description of water and aqueous solutions involves a number of physical observables, which characterize the macroscopic properties of the system. Numerical values can be assigned to these observables through conventional operations on macroscopic quantities of matter. Two representative examples are the viscosity — the ratio of shear stress to velocity gradient — and the relative permittivity — the ratio of capacitances with and without a ponderable medium between the plates of a capacitor. It is quantities such as these that contain — or, in a sense, conceal — the essential physics (as opposed to symmetry properties) within the framework of continuum theories such as hydrodynamics and electrostatics of dielectric media.

An important, and largely unresolved, question concerns the range of validity of the continuum representation of matter. For obscure reasons, continuum theory often makes numerically reasonable predictions even at the molecular level, where concepts such as viscosity and permittivity have lost much of their intuitive meaning. On the other hand, many fundamental phenomena cannot be explained without invoking the discrete nature of the medium and the specificity of intermolecular forces. It is at this point that chemistry enters — and destroys the beautiful simplicity of the continuum formalism.

The statistical-mechanical theory of the liquid state has seen major advances during the last decade. Yet, we still lack a comprehensive theory, which can quantitatively account for all the eccentricities of liquid water. Recent work — mainly computer simulation studies — has forced us to abandon the widely accepted structural models of ten years ago in favour of the vaguer description of water as a highly dynamic and imperfect network of tetrahedrally hydrogen-bonded molecules³. In the case of aqueous solutions the situation is even murkier. As Ninham⁴ recently put it: "Terms like 'hydrophobic interactions', 'ionic hydration', 'Stern layers', 'specific ion adsorption', 'structured water', and 'anomalous swelling', which have loomed large in the language of chemical physicists for half a century, have remained

unquantified. In a very real sense these terms are only slightly more advanced mnemonics than the electric atmospheres and magnetic effluvia of Descartes and his contemporaries."

Most aqueous systems of biological interest are heterogeneous, i.e., they contain macromolecules or molecular aggregates the dimensions of which greatly exceed those of a water molecule. A prominent feature of such systems is that interactions and dynamics involve a wide range of characteristic lengths and times. A complete description must necessarily include a bewildering assortment of phenomena; from proton jumps over 0.05 nanometer to Coulomb forces over tens of nanometers; from hydrogen-bond distortions with periods down to 0.05 picosecond to hindered water diffusion on a time-scale of tens of nanoseconds.

It is now generally recognized that the interaction of biological macromolecules and supermolecular assemblies with their aqueous environment is crucial for their structural integrity and biological function. This interaction has been investigated by a vast number of experimental techniques and theoretical approaches. Despite this trans-disciplinary effort — or, perhaps, because of it — the extent of general consensus regarding water-macromolecule interactions and dynamics is not particularly impressive. Not to mention the problem of intracellular water, where we are still in a situation which borders on metaphysics.

The protagonists of each one of the numerous sub-disciplines, which study water in biological systems, have developed their own vocabularies, which often embrace terms that might be included in Ninham's list. This problem of semantics is not a trivial one — after all, language is the vehicle of thought. One of the most widely used terms is that of "bound" water. This is a relevant concept for describing solid systems with very low water content, but it is misleading when used in connection with liquid aqueous solutions. To any chemist, the term "binding" conjures up a picture of an enthalpically driven and entropically opposed association process. Water, however, because of its solvent role, cannot be "bound" to a solute in this thermodyna-

mic sense. It simply occupies the available space. On the other hand, it is clear that the interaction between a solute and an individual water molecule differs from that between two water molecules. This fact has structural as well as dynamic implications.

The human brain has an amazing capacity for perceiving what we call order and structure. For this reason, these concepts appear intuitively simple and fundamental, but they are not easily quantified in simple and general terms. (Incidentally, this is the problem one faces when trying to program a computer for pattern recognition.) Consequently, it is important to explicitly define just what we mean by water structure, e.g., in terms of positional and angular distribution functions. Moreover, the structural characterization of hydration water must refer to the perturbation of a structural reference state: the hydrated water molecule. To the extent that this reference state is incompletely characterized, the structural aspects of hydration phenomena must, necessarily, remain somewhat obscure.

A complete description of the solute-induced perturbation of water structure must include two different aspects: extent and range. In other words; we want to know how many water molecules that are affected and how much. Since most experimental techniques operate on time-scales which are long compared to the time required for a water molecule to diffuse through the system one can obtain only average properties over all water molecules in the system. Unless the water content can be varied over a wide range without disturbing the integrity of the system (and even then the interpretation is not straightforward), the separation of extent from range can be accomplished only at the price of introducing specific models. Such models reflect not only the nature of the system under study, but also the sensitivity of the probing instrument. Consequently, the "hydration numbers" commonly cited in the literature must be regarded as operational quantities with limited intrinsic significance.

Through the perturbation of energetic barriers to molecular translation and reorientation, the solute-water interaction is

manifested also in dynamic properties. In fact, the dynamic perturbations are usually much more dramatic than the structural ones. Thus the mean residence times of water molecules directly coordinated to simple ions span some 12 orders of magnitude. As argued by Samoilov⁵, this fact demonstrates that it is meaningful to speak of "dynamically bound" water.

3. NUCLEAR MAGNETIC RESONANCE

3.1. Basic Principles

Most elements of the Periodic Table have at least one isotope with a nuclear magnetic moment. When such a nucleus is subjected to a magnetic field, its spin angular momentum (which is proportional to the magnetic moment) is quantized in space, i.e., it can adopt only certain orientations with respect to the external field. These orientations correspond to different energy levels of the spin system, between which transitions can be induced through absorption of electromagnetic radiation in the radio-frequency range. This is the basic phenomenon on which the technique of Nuclear Magnetic Resonance (NMR) is founded⁶.

A nucleus which has absorbed energy from the radiation field, does not remain in the excited spin state indefinitely. There exist a variety of relaxation mechanisms, whereby the spin system is brought back into thermal equilibrium with its molecular environment. These mechanisms involve various electromagnetic couplings between a spin and the rest of the system, e.g., molecular electron distributions or other spins. Since the rate of spin relaxation depends on, among other things, the rate at which the interaction fluctuates in time, relaxation rates contain information about the dynamics of molecular processes. In fact, there exists today no experimental technique that can rival NMR in versatility and selectivity in the study of molecular dynamics in aqueous systems.

The power of the NMR method derives partly from its gentleness; the energy involved is typically about one millionth of the thermal energy. Another strength is the weakness of the coupling of nuclear spins with molecular degrees of freedom. This fact — together with the elegant and powerful quantum-mechanical formalism for the description of spin — has made it possible to develop the theory of spin relaxation to a high level of sophistication and accuracy. This situation

may be contrasted with the formidable difficulties encountered in the analogous theory of dielectric relaxation.

Disregarding the radioactive ^3H nucleus, there are three water nuclei suitable for NMR studies: ^1H , ^2H , and ^{17}O . From the point of view of sensitivity, the proton and the deuteron are excellent NMR nuclei, whereas ^{17}O , with its low natural abundance (0.037 %) and high cost of enrichment, is less practical. Consequently, virtually all NMR studies of water in heterogeneous systems have utilized either ^1H or ^2H . However, during the last few years it has become clear that cross-relaxation, involving non-water protons, contributes to ^1H relaxation, thereby severely complicating the molecular interpretation⁷. Furthermore, it has been demonstrated that, in systems containing acidic functions, the molecular information obtained from ^1H and ^2H relaxation represents an irreducible average over water as well as non-water nuclei⁸. For these reasons and with the advent of computerized Fourier transform techniques⁹, which circumvent the sensitivity problem through extensive signal accumulation and the concomitant cancelling of noise, oxygen-17 now stands out as the most powerful nucleus for NMR studies of water in heterogeneous systems.

3.2. Multiexponential Relaxation

A technical problem encountered in ^{17}O NMR on heterogeneous systems is that the rate of decay of the macroscopic magnetization is not, in general, simply proportional to the instantaneous magnetization, as in a first-order kinetic process. This applies also to many nuclei of metal ions, e.g., ^{23}Na , ^{39}K , ^{25}Mg , and ^{43}Ca , which are finding increasing use in connection with biological systems¹⁰. The properties of these nuclei are such that if the fluctuations in the relaxing interaction are sufficiently slow, then the conventional types of NMR experiments cannot be analyzed in a simple way^{6,11}. Spin relaxation then becomes multiexponential, i.e., characterized, not by one, but several rate constants, and the data can be analyzed only with the aid of a computer.

In principle, the multitude of relaxation rates ought to be an advantage, since they provide more information about the molecular system than does a single one. In practice, however, it is often found that relaxation is singly exponential within the experimental accuracy. One is then left with a single apparent relaxation rate, from which molecular information can be extracted only after iterative computer calculations. This problem is treated in *paper I*, in which perturbation theory is used to derive simple analytical expressions for the rate of "nearly exponential" relaxation. These equations constitute excellent approximations for water ^{17}O relaxation in all heterogeneous systems studied here (Section 4).

The physical origin of the simplification can be traced back to the fast (relative to the relaxation) diffusion of water molecules, which leads to an observed relaxation behaviour representing a weighted average over all water molecules in the system. In any reasonable dilute heterogeneous system, the slow motions are effective in modulating the relaxing interaction of a particular spin only a small fraction of the time. Moreover, during that time only a small part of the interaction is fluctuating slowly (Section 3.3). Hence, the relative importance of the slow fluctuations (which are responsible for nonexponentiality) in determining the average relaxation behaviour is considerably reduced.

3.3. Relaxation in Heterogeneous Systems

In order to interpret spin relaxation data, one needs a physical model for the relevant molecular motions in the system. This model should be simple, i.e., contain as few adjustable parameters as possible, and general, i.e., it should be applicable to relaxation in isotropic as well as in macroscopically anisotropic systems and to all three magnetic water nuclei (^1H , ^2H , and ^{17}O). In *paper II*, such a model is formulated and used to derive relaxation equations applicable to heterogeneous systems. The treatment constitutes an elaboration and generalization of the relaxation theory presented by Wennerström in 1974 with special emphasis on nuclei of simple ions¹². To motivate the model, it is useful to identify the indisputable experimental facts from NMR studies of water nuclei in heterogeneous systems.

Consider first an aqueous region adjacent to an immobile, although not necessarily rigid, surface. Typical examples include phospholipid bilayers, surfactant liquid-crystalline mesophases, clays, and protein crystals. Such systems have been studied extensively — using all three water nuclei — during the past few decades and two important conclusions have been drawn: (1) the NMR absorption lines exhibit splittings, indicating a preferential water orientation relative to the surface, and (2) the splittings are much smaller than expected for rigid attachment of water to the surface, i.e., the orientational bias is small. This is qualitatively what one would predict on the basis of the current theoretical understanding of water-water and water-surface interactions.

Let us now focus our attention on a different kind of system, e.g., a dilute aqueous solution of a globular protein. The most important experimental observation in these isotropic systems is the frequency dependence of the relaxation rates. (The inequality of longitudinal and transverse relaxation rates may also be regarded as a frequency dependence.) The form of this frequency dependence implies that the relaxation is induced by molecular motions on two time-scales; typically

the slow one is in the nanosecond range, while the fast one is in the picosecond range. The main source of controversy in the water NMR literature of recent years concerns the nature of these motions and the mechanism whereby they induce spin relaxation.

There can be little doubt that the local environment of a water molecule in the immediate neighbourhood of a protein surface is very similar to that in the previously discussed macroscopically anisotropic systems. The fast motion can thus be identified with local water tumbling and side chain libration.

The characteristic times for fluctuations in the relaxing interaction are given by so-called correlation times. Loosely speaking, these quantities measure the time that a water molecule "remembers" its orientation relative to the external magnetic field. The fast local reorientation will cause a water molecule to lose most of its orientational "memory" very quickly. But because of the slight average orientational bias — quantified by the so-called residual anisotropy, which involves certain order parameters — the water molecules near the protein surface will also have a "long-term memory". In the case of the immobile surface, this gives rise to a line splitting, whereas in a protein solution, the "long-term memory" is washed out by slow motions (e.g. protein tumbling) thereby producing a frequency dependence in the relaxation.

The fast motion can thus be referred to fluctuations in the orientation of a water molecule relative to the protein surface, and the slow motion to fluctuations in the orientation of the local constraint axis or director relative to the external field. This step-wise loss of orientational "memory" or correlation — characterized by a fast and a slow correlation time and by the residual anisotropy — constitutes the essence of the so-called two-step model for spin relaxation in heterogeneous systems, as presented in paper II. Above all, it is the occurrence of molecular motions on disjoint time-scales that guarantees a simple result with independent contributions to the relaxation rate from the

two classes of motion. Incidentally, time-scale separation has simplified life in many branches of physics; the Born-Oppenheimer approximation is a familiar example.

If hydration water is regarded as "dynamically bound", then it is clearly important to establish the mean residence time of water molecules in the hydration region. If we continue to discuss the dilute protein solution, then there are at least two types of motion which could obliterate the "long-term memory". The most obvious one is protein tumbling, which modulates the orientation of the local director with respect to the external field. However, the same result can be accomplished also by translational diffusion of water molecules from one protein molecule to another. The correlation time for this latter process ("chemical exchange" in the NMR jargon) provides the desired measure of the lifetime or residence time. When both processes are operative, the rate of the slow fluctuation is given by the sum of the two independent rates of protein tumbling and water exchange. If the protein is sufficiently large, it will tumble so slowly that a "dynamically bound" water molecule will diffuse away into the bulk before the protein has reoriented appreciably. In that case, the measured slow correlation time equals the lifetime. This way of deducing the lifetime may be viewed as a kind of self-diffusion measurement, in which a water molecule is labelled by the orientation of its local constraint axis.

It may be argued that there should be a third contribution to the slow fluctuation, namely surface diffusion. But as long as a bulk water phase exists, a water molecule which is "dynamically bound" to a charged residue on a protein surface probably experiences an equally high diffusional barrier along the surface as perpendicular to it. Hence water surface diffusion can be neglected in dilute systems. However, in the case of strongly hydrated counterions, e.g., Li^+ or Mg^{2+} , the counterion hydration sheath may be sufficiently long-lived for these water molecules to be effectively trapped with the ions.

3.4. Proton Transfer and Scalar Relaxation

The spin relaxation of ^{17}O nuclei in liquid water can proceed via two different mechanisms. These are termed quadrupolar and scalar relaxation and are induced by water tumbling (Section 3.3) and O-H bond disruption, respectively. In pure water under ordinary conditions, a given water molecule remains intact, on the average, about 11 hours before dissociating spontaneously. Chemical transformation of water molecules can also be induced by various acidic or basic catalysts – the most important being the prototropic ions H_3O^+ and OH^- . For this reason, the rate of ^{17}O (and ^1H) relaxation in water is pH-dependent. Twenty years ago, Meiboom¹³ recognized in this fact a possibility to study – more directly than by means of electric conductivity measurements – the intriguing phenomenon of prototropic charge transport in water. The relaxation theory relevant to such studies is revised and extended in *paper VI*.

In aqueous solutions of macromolecules or molecular aggregates, there is commonly an abundance of acidic and basic chemical functions, which may exchange protons with the solvent molecules. The rate of proton exchange catalyzed by surface groups can be extremely high, far exceeding that in the bulk water phase. A water molecule initially in the bulk phase may then exchange one of its protons via either of two paths: (1) through an encounter with a prototropic ion in the bulk (at a known pH-dependent rate), or (2) via diffusion to the surface, surface-catalyzed proton exchange, and subsequent diffusion back into the bulk. The rate of the latter pathway is limited by the surface-catalyzed proton exchange rate or by the rate of water molecule departures from the catalyzing surface groups – whichever is the slowest. On the basis of this phenomenon, a new method of obtaining limits to "dynamically bound" water lifetimes was developed and applied in *paper IV*.

4. WATER STRUCTURE AND DYNAMICS IN HETEROGENEOUS SYSTEMS

4.1. Surfactant Micelles

While ionic and polar substances readily dissolve in water, nonpolar substances, such as hydrocarbons, are virtually insoluble. A mixture of comparable quantities of water and hydrocarbon is therefore thermodynamically unstable and eventually separates into two phases, in each of which the molecules are surrounded by their own kind. (Unfortunately, there is an anthropomorphic analogy.)

There occurs in Nature also an intriguing kind of hybrid molecules. Incorporating a nonpolar as well as an ionic or polar part, these molecules are termed amphiphiles. Among the more prominent amphiphiles we find surfactants and phospholipids, chief constituents of detergents and biological membranes, respectively. When confronted with an aqueous environment, these molecules satisfy their schizophrenic solubility requirements by forming aggregates. A whole hierarchy of structures can result, the simplest one being the micelle; a spherical or cylindrical aggregate of from around ten up to hundreds of amphiphilic molecules.¹⁴ The amphiphiles are arranged so that their ionic "head-groups" reside at the micelle surface in contact with the aqueous medium, whereas their nonpolar "tails" are buried in the interior of the micelle.

Although surfactant association into micelles has been studied since the turn of the century¹⁵, it is only fairly recently that it has become generally recognized that the driving force for surfactant association is inherent in the structure of water¹⁶. Furthermore, we now know that the same phenomenon — usually called the hydrophobic interaction — is responsible, to a large extent, for the structural organization of living systems. While of considerable intrinsic interest, surfactant micelles thus furnish also well-defined model systems, the study of which has far-reaching biological implications.

One of the most fundamental — and least understood — aspects of micellar solutions is the molecular details of the water-micelle

interaction. This state of affairs motivated the work reported in *paper III*. Aqueous solutions of a variety of ionic surfactant micelles were investigated by ^{17}O NMR, allowing structural and dynamic information to be extracted. The results confirmed the, recently challenged, classical picture¹⁷ of micelles as having a hydrocarbon interior with very little contact with the aqueous medium. The importance of the nature of headgroup and counterion in perturbing the surrounding water molecules was also assessed. Furthermore, it was shown that whereas the "dynamically bound" water molecules reorient quite rapidly, their mean residence time at the micelle surface is comparatively long; on the order of ten nanoseconds.

4.2. Linear Polyelectrolytes

Polyelectrolytes are polymeric molecules, the monomers of which carry net electric charge in aqueous solution. Since the charge is acquired through the loss or gain of a proton, the total amount of charge on the polymer can be controlled by variation of the solution pH. Polyelectrolytes built from repeating units with the same charge are forced, by electrostatic repulsion, to adopt open, extended conformations. Such linear polyelectrolytes are widely distributed in Nature in the form of nucleic acids, polyphosphates, and mucopolysaccharides, to name but a few. Periodic linear polyelectrolytes are readily synthesized and have found diverse technical applications. Synthetic polyelectrolytes in aqueous solution have been extensively studied during the last three decades with particular emphasis on chain conformation and counterion distribution¹⁸. The aim of *paper IV* was to supplement the current rather detailed picture of polyelectrolyte solutions with structural and dynamic information about the aqueous component.

Oxygen-17 relaxation rates were measured in aqueous solutions of poly(acrylic acid) (PAA) and poly(methacrylic acid) (PMA) — the two most well-documented synthetic polyelectrolytes. The results were similar to those obtained from micellar solutions (Section 4.1), i.e., "dynamically bound" water molecules tumble rapidly (about an order of magnitude slower than in pure water) and are perturbed mainly by the anionic carboxylate groups. Additional insight about the polyelectrolyte - water interaction was obtained by varying the degree of ionization of the polyacids. Thus it was found that even water molecules "dynamically bound" to protonated carboxylic groups have residence times on the order of ten nanoseconds. Consequently, long water lifetimes are not necessarily due to counterion "condensation", as might have been the case in the micellar solutions.

Chemically, PAA and PMA differ merely in that PMA contains an additional methyl group per monomer. This minute difference has

profound consequences for the conformational state at low charge densities, where the reduced electrostatic repulsion permits chain segments to come into contact. In addition to water dynamics, the ^{17}O data also provided information about the polymer motions, in agreement with results obtained by other methods, e.g., ^{23}Na counterion NMR¹⁹.

4.3. Globular Proteins

The nature of water in biological systems, e.g., protein solutions or intact cells, is a unique problem in two respects: the huge amount of work that has been invested and the striking disagreement and controversy concerning the interpretation of the results.^{20,21} Thus the hydration water of globular proteins has been variously described as "ice-like", "non-freezable", "irrotationally bound", etc. However, the interpretation of much of the early work — be it hydrodynamic, dielectric, or NMR data — lacked a sound theoretical basis. In the case of NMR, for example, it has become clear that the interpretation of water ^1H and ^2H relaxation rates from protein solutions is less straightforward than generally believed a few years ago (Section 3.1).

Oxygen-17 NMR data from seven aqueous protein solutions, reported in *paper V*, demonstrate the inadequacy of previous relaxation models and provide strong support for the "two-step" model (Section 3.3). It is reassuring to find that in micelle, polyelectrolyte, and protein solutions alike, the perturbation of the aqueous medium is small (the tumbling rate of "dynamically bound" water is slowed down less than an order of magnitude as compared to pure water) and short-ranged and that ionic residues produce larger perturbations than do uncharged ones.

The variation of the global "hydration" among the various proteins studied was found to be largely a consequence of the difference in the density of ionic residues at the surface. It should be stressed, however, that in a two-state model one obtains only average properties of several hundred interacting water molecules. To understand the involvement of hydration in the biological function of enzymes, it is of course necessary to have much more detailed information. One possible way to obtain such information appears to be by means of scalar ^{17}O relaxation, which, under favourable circumstances, can selectively monitor one or a few water molecules in the active site of an enzyme (P. Brand and B. Halle, unpublished results).

In the work described in paper V, no "dynamically bound" water lifetimes were established. However, the slow correlation times in the range 10 - 25 nanoseconds may be regarded as approximate lower limits for the lifetimes. This is of the same order of magnitude as was found for ionic micelles and polyelectrolytes. It appears unlikely that water should be associated with proteins much longer than with, for example, micelles, since the surface structure and dynamics is similar. The obvious way to settle this question is to measure ^{17}O relaxation rates in solutions of very large proteins (Section 3.3). Unfortunately, the ^{17}O dispersion data reported in paper V include only relatively small proteins. However, the linewidths from the two largest ones (alcohol dehydrogenase and immunoglobulin G) are strongly indicative of a lifetime on the order of 10^{-8} seconds. Thus immunoglobulin G, being nearly twice as large as alcohol dehydrogenase, should reorient nearly an order of magnitude slower, whereas the observed transverse relaxation enhancement is merely 15 % larger. The dispersion in the microsecond range, obtained from ^1H and ^2H NMR in solutions of large proteins²², is thus most likely due to exchangeable protons or deuterons.

5. PROTOTROPIC CHARGE TRANSPORT IN WATER

What commonly is referred to as "pure water" is actually a dilute solution of the ionic dissociation products of water: the hydroxide ion and the proton. The latter, being an "elementary" particle (let's forget about quarks for the moment), is a very special chemical entity. In fact, it does not exist in aqueous solution, but combines with a water molecule to form the symmetric hydronium ion.²³ (The instability of the free proton may be illustrated by the fact that in 10^{70} universes filled with 1 molar acid solution, there would be only one free proton.)

The prototropic ions, H_3O^+ and OH^- , have striking properties not exhibited by other ions. This is a consequence of their relation to the solvent water. Thus it has been known for well over a century that prototropic ions are much more effective than other ions in transporting electric current through aqueous solutions. In 1905, it was suggested that this anomalous electric conductivity has its origin in rapid proton transfer between prototropic ions and neighbouring water molecules.²⁴ Through this mechanism, charge can be transported at a rate which is considerably higher than that of diffusion of the massive charge-carriers themselves. Even though this ingenious idea turned out to be correct, the task of formulating a comprehensive theoretical model for prototropic charge transport in water has remained a major challenge to physical chemists to this day.²⁵

This problem is considered in *paper VI*, which is already far too voluminous — so I shall not waste more words on it here.

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Sometimes I wonder why I am wasting my few years in the present incarnation on such inessentials as nuclear spins and water molecules. The answer, I suspect, has not so much to do with the noble aims of science as with the open and friendly atmosphere created by ALL of my colleagues in the physical chemistry departments in Lund.

There are, however, two persons who have especially influenced my work during these years:

BJÖRN — who put me on the ^{17}O track and kept me at it through continuous and generous support and encouragement, and

HÅKAN — whose profound insight and unselfish attitude has taught me what I could not learn from textbooks.

I am also deeply indebted to Bengt, Göran, Hans, and Sture, whose exuberant enthusiasm was instrumental in getting me addicted to science, and to Bo, Gunnar, Göran, Lennart, Sven, and Thomas for amiable and rewarding cooperation. And to Aatto: thank J_{OH} .

Many thanks go also to Bodil, Eva, and Ingegerd for help with typing and drawing.

Last — and, perhaps, least — I thank the Swedish taxpayers for financing these years of amusement.

With two lines from Byron I conclude:

*'Tis pleasant, sure, to see one's name in print;
A book's a book, although there's nothing in't.*

I

Nearly Exponential Quadrupolar Relaxation. A Perturbation Treatment

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Quadrupolar nuclear spin relaxation is treated by a perturbation method, which shows that the relaxation is nearly exponential provided that the effective spectral density is only weakly frequency dependent. Approximate analytical expressions for the relaxation rates are derived and tested against the experimentally accessible apparent relaxation rates, for a fast-exchange two-state model. The results for spin $I = 5/2$ and $7/2$ indicate that the analytical expressions are accurate to within a few percent in most experimental situations.

INTRODUCTION

The magnetic relaxation of a nucleus with spin $I \geq 1$ is usually due mainly to the interaction of the nuclear electric quadrupole moment with fluctuating electric field gradients present at the position of the nucleus. It was shown 25 years ago (1) that, except for the case $I = 1$, which will not concern us here, quadrupolar relaxation is, in general, not a simple exponential decay. For nuclei with half-integral spin, such as ${}^7\text{Li}$, ${}^{23}\text{Na}$, ${}^{35}\text{Cl}$, ${}^{39}\text{K}$ ($I = 3/2$), ${}^{17}\text{O}$, ${}^{25}\text{Mg}$ ($I = 5/2$), ${}^{43}\text{Ca}$, ${}^{133}\text{Cs}$, and ${}^{139}\text{La}$ ($I = 7/2$), the magnetization decays as a weighted sum of $I + 1/2$ exponentials. For $I = 3/2$ there exist analytical expressions (1, 2) for the two relaxation rates, whereas for $I = 5/2$ and $7/2$ the relaxation matrix has to be diagonalized numerically. This has been done in a series of papers (3–6) dealing with the completely analogous case of electron spin relaxation by modulation of the quadratic zero-field splitting, which, like the quadrupole coupling, is a second-rank interaction, and, more recently, also in connection with nuclear quadrupole relaxation (7, 8).

In recent years, nuclear magnetic relaxation of quadrupolar nuclei has been used extensively to obtain information on the interaction of ions and small molecules with macromolecules and large molecular aggregates (9–12). In many cases, the observed nuclei are involved in rapid chemical exchange between a “bound” state, where there is significant interaction with the macromolecule or aggregate, and a “free” state, where fast reorientation makes the “extreme narrowing” approximation (the spectral density of the fluctuating field gradient is constant up to twice the resonance frequency) valid. In the bound state, however, extreme narrowing conditions do not usually obtain, with the result that the relaxation becomes multiexponential.

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Pronounced deviations from simple exponential decay and Lorentzian absorption lineshape, a prerequisite for a full nonexponential analysis, have, to our knowledge, been observed only for ^{23}Na (13–18). More commonly, the relaxation appears exponential, even when the contribution from the bound state is considerable and when the longitudinal and transverse relaxation rates are unequal and frequency dependent. Clearly, approximate analytical expressions for the apparent longitudinal and transverse relaxation rates in this regime of “nearly exponential” relaxation would be very useful. This is particularly so for $I = 5/2$ and $7/2$, where, otherwise, the relaxation matrix must be diagonalized numerically for each set of values for the spectral densities, and apparent relaxation rates then calculated from a fit to a simple exponential decay or from the linewidth of the actual superposition of Lorentzians.

We approach the problem of obtaining approximate analytical expressions for the relaxation rates through a perturbation treatment, in which we regard the extreme narrowing situation as being “perturbed” by allowing for a frequency dependence in the spectral density. In order to assess the validity of the resulting equations, we present numerical results for $I = 3/2, 5/2$, and $7/2$.

MULTIEXPONENTIAL SPIN RELAXATION IN MATRIX FORMALISM (19, 20)

In the basis of eigenvectors of the Zeeman Hamiltonian, the longitudinal ($\alpha = 1$) and transverse ($\alpha = 2$) components of the macroscopic magnetization may be written

$$M_\alpha(t) = N\gamma\hbar \tilde{\mathbf{I}}_\alpha \chi_\alpha(t), \quad [1]$$

where $M_1(t) \equiv M_z(t) - M_{\text{eq}}$ and $M_2(t) \equiv M_+^*(t)$. The $\tilde{\mathbf{I}}_\alpha$ are column vectors (tilde denotes transposition) representing spin operators and have components $I_{1,m} = m$ and $I_{2,m} = [I(I+1) - m(m+1)]^{1/2}$, respectively. The χ_α are column vectors composed of matrix elements of the reduced density operator according to $\chi_{1,m} = \chi_{mm} - \chi_{-m-m}$ and $\chi_{2,m} = \chi_{mm+1}^I$, the superscript referring to the interaction representation.

The time evolution of the vectors $\chi_\alpha(t)$ is, under certain conditions, given by Redfield's equation of motion in the Zeeman basis,

$$\frac{d}{dt} \chi_\alpha(t) = -\mathbf{R}_\alpha \chi_\alpha(t), \quad [2]$$

with the formal solution

$$\chi_\alpha(t) = \exp[-\mathbf{R}_\alpha t] \chi_\alpha(0). \quad [3]$$

The elements of the square matrices $\mathbf{R}_\alpha$ are related to the elements of the conventional relaxation matrix through $R_{1,mn} = R_{mm-n-n} - R_{mnnn}$ and $R_{2,mn} = -R_{mm+1nn+1}$. For half-integral spin, the dimension of the vector space is $I + 1/2$ ($m = 1/2, 3/2, \dots, I$) for $\alpha = 1$ and $2I$ ($m = -I, -I+1, \dots, I-1$) for $\alpha = 2$.

The symmetric relaxation matrices $\mathbf{R}_\alpha$ are diagonalized by orthogonal transformation matrices $\mathbf{S}_\alpha$,

$$\mathbf{R}_\alpha^S = \mathbf{S}_\alpha \mathbf{R}_\alpha \hat{\mathbf{S}}_\alpha. \quad [4]$$

The columns of $\tilde{\mathbf{S}}_\alpha$ constitute the eigenvectors $\mathbf{S}_{\alpha k}$ of $\mathbf{R}_\alpha$ with eigenvalues $R_{\alpha k}$,

$$\mathbf{R}_\alpha \mathbf{S}_{\alpha k} = R_{\alpha k} \mathbf{S}_{\alpha k}. \quad [5]$$

Equations [1], [3], and [4] yield the solution

$$M_\alpha(t) = M_\alpha(0) [\tilde{\mathbf{I}}_\alpha \mathbf{I}_\alpha]^{-1} \tilde{\mathbf{I}}_\alpha^S \exp[-\mathbf{R}_\alpha^S t] \mathbf{I}_\alpha^S, \quad [6]$$

where use has been made of the proportionality $\chi_\alpha(0) \propto \mathbf{I}_\alpha$ and where $\mathbf{I}_\alpha^S = \mathbf{S}_\alpha \mathbf{I}_\alpha$ is the spin vector transformed to the eigenbasis of $\mathbf{R}_\alpha$. Equation [6] may be rewritten as

$$M_\alpha(t) = M_\alpha(0) \sum_{k=1}^{I+1/2} c_{\alpha k} e^{-R_{\alpha k} t}, \quad [7]$$

where the normalized amplitudes are defined by

$$c_{\alpha k} \equiv [\tilde{\mathbf{I}}_\alpha \mathbf{I}_\alpha]^{-1} [\tilde{\mathbf{S}}_{\alpha k} \mathbf{I}_\alpha]^2. \quad [8]$$

Equation [7] shows that the magnetization decays as a weighted sum of $I + 1/2$ exponentials. This is true also in the transverse case, since the $2I$ -dimensional $\mathbf{R}_2$ matrix can be transformed to block-diagonal form by exploiting the invariance of $\mathbf{I}_2$ and $\mathbf{R}_2$ with respect to the replacement $m \rightarrow -m - 1$. The transverse relaxation is then described by the largest block, of dimension $I + 1/2$.

The simple exponential decay obtained for extreme narrowing emerges since, in that case, $\mathbf{I}_\alpha$ is proportional to an eigenvector of $\mathbf{R}_\alpha$. According to Eq. [8], only one of the amplitudes $c_{\alpha k}$ is then nonzero. For nonextreme narrowing this is no longer true and it becomes necessary to determine the eigenvalues and eigenvectors of the relaxation matrices. For $I = 3/2$ this can be accomplished analytically (1, 2), whereas for $I = 5/2$ and $7/2$ one must, in the general case, rely on numerical methods. However, for practical purposes it is desirable to have approximate analytical expressions for the relaxation behavior.

PERTURBATION TREATMENT

As a first step in determining approximate eigenvalues and eigenvectors of the relaxation matrices, we make the transformation

$$\mathbf{R}_\alpha^{S_0} = \mathbf{S}_\alpha^{(0)} \mathbf{R}_\alpha \tilde{\mathbf{S}}_\alpha^{(0)}. \quad [9]$$

where $\mathbf{S}_\alpha^{(0)}$ defines the transformation that diagonalizes $\mathbf{R}_\alpha$ for extreme narrowing conditions; $\mathbf{S}_\alpha^{(0)}$ depends only on α and I and can be obtained in analytical form. There are two points worth noting about the transformation [9]. First, if the deviation from extreme narrowing is small, then $\mathbf{R}_\alpha^{S_0}$ will be "nearly diagonal." Second, one of the columns of $\tilde{\mathbf{S}}_\alpha^{(0)}$ is proportional to $\mathbf{I}_\alpha$.

From Tables 1 and 2, which show the transformed relaxation matrices $\mathbf{R}_\alpha^{S_0}$ for $I = 5/2$ and $7/2$, respectively, it is seen that the off-diagonal elements are determined by differences between spectral densities at frequencies 0, ω_0 , and $2\omega_0$. Thus, for extreme narrowing, i.e., when $J(\omega)$ is independent of ω , the matrices correctly reduce to diagonal form (with elements that are independent of α). Here, and in the following, we assume that the Hamiltonian describing the mo-

TABLE I
TRANSFORMED RELAXATION MATRICES FOR $I = 5/2$

$\mathbf{R}_\alpha^{S_0} = K \begin{bmatrix} A & E & 0 \\ E & B & F \\ 0 & F & C \end{bmatrix}, \quad K = \frac{3}{125} \left[\frac{eQ}{\hbar} \right]^2$		
	$\alpha = 1$	$\alpha = 2$
A	$2J_1 + 8J_2$	$3J_0 + 5J_1 + 2J_2$
B	$\frac{1}{4}(82J_1 + 83J_2)$	$\frac{1}{24}(123J_0 + 370J_1 + 497J_2)$
C	$\frac{25}{4}(2J_1 + J_2)$	$\frac{5}{12}(3J_0 + 26J_1 + 16J_2)$
E	$-\frac{18}{(14)^{1/2}}(J_1 - J_2)$	$\frac{27}{2(21)^{1/2}}(J_0 - J_2)$
F	$-\frac{125}{2(35)^{1/2}}(J_1 - J_2)$	$-\frac{25}{12(14)^{1/2}}(3J_0 + 14J_1 - 17J_2)$

molecular motion is invariant under rotations. The relaxation matrix elements then contain spectral densities of the form (19)

$$J_q \equiv J_{00}(q\omega_0) = \frac{1}{4} \int_{-\infty}^{\infty} d\tau e^{-iq\omega_0\tau} \langle V_{zz}^L(0) \dot{V}_{zz}^L(\tau) \rangle, \quad [10]$$

where V_{zz}^L is the second partial derivative, with respect to the laboratory-fixed z coordinate, of the electric potential at the position of the nucleus.

If all off-diagonal elements $R_{\alpha l k}^{S_0}$ are small relative to the difference between the diagonal elements which they connect, then approximate eigenvalues and eigenvectors of $\mathbf{R}_\alpha$ can be obtained through a perturbation expansion. To first order, the eigenvalues are simply the diagonal elements of $\mathbf{R}_\alpha^{S_0}$ with corresponding eigenvectors (21),

$$S_{\alpha k}^{(1)} = S_{\alpha k}^{(0)} + \sum_{l \neq k} \frac{R_{\alpha l k}^{S_0}}{R_k^{(0)} - R_l^{(0)}} S_{\alpha l}^{(0)}, \quad [11]$$

where the $R_k^{(0)}$ denote the zeroth-order eigenvalues, i.e., $R_{\alpha k k}^{S_0}$ for $J(\omega)$ independent of ω and where the $S_{\alpha k}^{(0)}$ are the columns of $\tilde{\mathbf{S}}_\alpha^{(0)}$. On inserting this expression into Eq. [8] one obtains for the (unnormalized) amplitudes

$$c_{\alpha k}^{(1)} = [\tilde{\mathbf{I}}_\alpha \mathbf{I}_\alpha]^{-1} \left[\tilde{\mathbf{S}}_{\alpha k}^{(0)} \mathbf{I}_\alpha + \sum_{l \neq k} \frac{R_{\alpha l k}^{S_0}}{R_k^{(0)} - R_l^{(0)}} \tilde{\mathbf{S}}_{\alpha l}^{(0)} \mathbf{I}_\alpha \right]^2. \quad [12]$$

Since $\mathbf{I}_\alpha$ is proportional to the first column of $\tilde{\mathbf{S}}_\alpha^{(0)}$ we have $\tilde{\mathbf{S}}_{\alpha k}^{(0)} \mathbf{I}_\alpha = \delta_{k1} [\tilde{\mathbf{I}}_\alpha \mathbf{I}_\alpha]^{1/2}$

and consequently

$$\begin{aligned} c_{\alpha 1}^{(1)} &= 1, \\ c_{\alpha 2}^{(1)} &= \left[\frac{R_{\alpha, 12}^{S_0}}{R_2^{(0)} - R_1^{(0)}} \right]^2, \\ c_{\alpha k}^{(1)} &= 0, \quad k > 2, \end{aligned}$$

[13]

where use has been made of the fact that only one-off-diagonal elements of $\mathbf{R}_\alpha^{S_0}$ are nonzero (see tables).

Thus, to first order the relaxation is biexponential and the relaxation rate of the major component, corresponding to element A in the tables, is

$$R_{11}^{(1)} = \frac{3}{40} \left[\frac{eQ}{\hbar} \right]^2 \frac{2I + 3}{I^2(2I - 1)} [2J_1 + 8J_2],$$

[14a]

$$R_{21}^{(1)} = \frac{3}{40} \left[\frac{eQ}{\hbar} \right]^2 \frac{2I + 3}{I^2(2I - 1)} [3J_0 + 5J_1 + 2J_2],$$

[14b]

where eQ is the nuclear electric quadrupole moment. It is interesting to note that

TABLE 2
TRANSFORMED RELAXATION MATRICES FOR $I = 7/2$

$$\mathbf{R}_\alpha^{S_0} = K \begin{bmatrix} A & E & 0 & 0 \\ E & B & F & 0 \\ 0 & F & C & G \\ 0 & 0 & G & D \end{bmatrix}, \quad K = \frac{1}{98} \left[\frac{eQ}{\hbar} \right]^2$$

	$\alpha = 1$	$\alpha = 2$
A	$2J_1 + 8J_2$	$3J_0 + 5J_1 + 2J_2$
B	$2(12J_1 + 13J_2)$	$\frac{11}{3} \left(\frac{18}{11} J_0 + 5J_1 + 7J_2 \right)$
C	$\frac{10}{13} (53J_1 + 51J_2)$	$\frac{1}{39} (159J_0 + 1427J_1 + 1534J_2)$
D	$\frac{28}{13} (8J_1 + 5J_2)$	$\frac{11}{13} \left(\frac{12}{11} J_0 + 19J_1 + 13J_2 \right)$
E	$-\frac{44}{(77)^{1/2}} (J_1 - J_2)$	$\frac{3(22)^{1/2}}{(21)^{1/2}} (J_0 - J_2)$
F	$-\frac{40(13)^{1/2}}{(77)^{1/2}} (J_1 - J_2)$	$-\frac{52(5)^{1/2}}{3(2002)^{1/2}} (3J_0 + 14J_1 - 17J_2)$
G	$-\frac{1960}{13(77)^{1/2}} (J_1 - J_2)$	$\frac{42(35)^{1/2}}{(39,039)^{1/2}} (J_0 + 12J_1 - 13J_2)$

the same expressions are valid for the initial relaxation rates, defined by

$$R_\alpha(0) \equiv - \frac{1}{M_\alpha(0)} \left. \frac{dM_\alpha(t)}{dt} \right|_{t=0}. \quad [15]$$

This is most directly shown by evaluating the operator equations [130] and [131] of Chap. VIII in Abragam's treatise (19). The analogous equations, for the case of electron spin relaxation, have previously been derived by McLachlan (22), who also noted that the initial rates, $R_\alpha(0)$, may be regarded as average relaxation rates in the sense

$$\langle R_\alpha \rangle = \sum_{k=1}^{I+1/2} c_{\alpha k} R_{\alpha k}. \quad [16]$$

The equality of $R_\alpha(0)$ and $\langle R_\alpha \rangle$ follows directly from Eqs. [7] and [15]. Expressions [14] have been obtained, for the special case of $I = 3/2$, in yet another way by Bull (23), who linearized the analytic expressions for $I = 3/2$ in the time variable.

According to the perturbation treatment, the initial rates actually apply over the entire decay, provided that the spectral density is only weakly frequency dependent. The rate of convergence of the perturbation expansion and thus the accuracy of a description of the relaxation behavior as a simple exponential decay with a rate given by Eq. [14] may be investigated by proceeding to higher orders and making an assumption about the functional form of the frequency dependence of $J(\omega)$. However, experimentally one does not measure the rates, $R_{\alpha 1}$, to which Eq. [14] is an approximation, but rather apparent relaxation rates R_α^* obtained from the absorption line width or from an exponential least-squares fit to the decay following certain pulse sequences. It is therefore more useful to assess the validity of expressions [14] in relation to the apparent rates R_α^* .

CALCULATIONS

We consider a nucleus which is part of a species that exchanges rapidly, relative to the relaxation rates, between a "bound" state (B) and a "free" state (F). The effective spectral density is then a weighted average of the individual spectral densities,

$$J_q = P_F J_q^F + P_B J_q^B, \quad [17]$$

where P_F and P_B are the relative populations of the two states. In most cases of interest, the observed nucleus resides in an ion or in a water molecule (^{17}O) in an aqueous solution containing macromolecules or large molecular aggregates. The F state then corresponds to the bulk of the solution, where it is reasonable to assume that $J_q^F = J_0^F$. In the B state, however, the probe experiences the slower motion of the macromolecule so that the spectral density may become frequency dependent. If we assume that the correlation function in Eq. [10] decays exponentially, corresponding to isotropic motion, with a correlation time τ_{cB} , then

$$J_q^B = \frac{1}{10} (V_{zz}^M)^2 \left[1 + \frac{\eta^2}{3} \right] \frac{e^{-\tau_{\text{cB}}}}{1 + (q\omega_0\tau_{\text{cB}})^2}, \quad [18]$$

where V_{zz}^M and η have their usual meanings (19). Due to the frequency-independent term in [17], the relative variation of the spectral density with frequency will be smaller and the first-order result [14] is expected to be valid over a fairly wide range of conditions.

On inserting [17] and [18] into Eq. [14] we obtain

$$\frac{\langle R_1 \rangle}{P_F R_F} = 1 + Q[0.2\bar{J}_1^B + 0.8\bar{J}_2^B], \quad [19a]$$

$$\frac{\langle R_2 \rangle}{P_F R_F} = 1 + Q[0.3 + 0.5\bar{J}_1^B + 0.2\bar{J}_2^B]. \quad [19b]$$

Here, and in the following, we use the symbol $\langle R_\alpha \rangle$ to denote the rates given by Eq. [14]. In [19] we have introduced two dimensionless quantities

$$\bar{J}_q^B \equiv \frac{J_q^B}{J_0^B} = [1 + (q\omega_0\tau_{CB})^2]^{-1}, \quad [20]$$

$$Q \equiv \frac{P_B \chi_{eB}^2 \tau_{CB}}{P_F \chi_{eF}^2 \tau_{CF}}, \quad [21]$$

where the effective quadrupole coupling constant is defined by

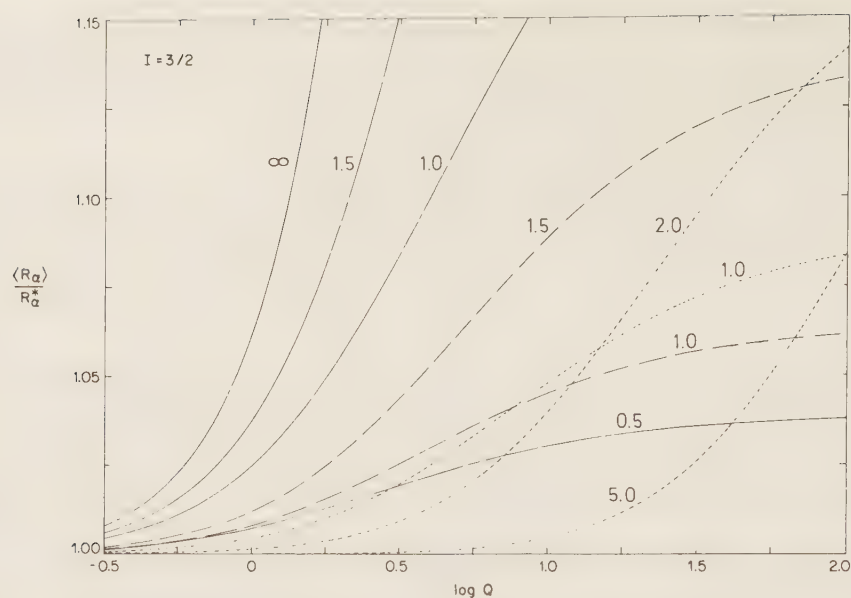
$$\chi_e \equiv \frac{|eQV_{zz}^M|}{h} \left[1 + \frac{\eta^2}{3} \right]^{1/2}. \quad [22]$$

Thus, $\langle R_\alpha \rangle / P_F R_F$, as well as the "reduced" relaxation matrix $\mathbf{R}_\alpha / P_F R_F$, are completely determined by the system parameter Q and the instrumental (for fixed τ_{CB}) parameter $\omega_0\tau_{CB}$. The slow-exchange limit (B state observed) obtains when Q becomes so large that unity is negligible compared to the second term in Eq. [19].

Reduced apparent relaxation rates $R_\alpha^* / P_F R_F$ were obtained, for given values of Q and $\omega_0\tau_{CB}$, through numerical diagonalization of the full relaxation matrices. With the resulting $c_{\alpha k}$ and $R_{\alpha k} / P_F R_F$ we then calculated apparent rates from the linewidth of the $I + 1/2$ superposed Lorentzians (R_2^{*a}) or from a least-squares fit of a simple exponential decay to ten points, equally spaced in magnetization from $0.95 M_\alpha(0)$ to $0.05 M_\alpha(0)$, taken from the $(I + 1/2)$ -exponential decay (R_α^{*e}).

Figures 1–3 illustrate the error made by equating the various apparent relaxation rates, R_1^{*e} , R_2^{*e} , or R_2^{*a} , to the corresponding first-order relaxation rate $\langle R_\alpha \rangle$ as given by Eq. [14]. First we may note that the approximation improves considerably in going from $I = 3/2$ to $5/2$. Increasing I to $7/2$ results in a further slight improvement. The error in the longitudinal rate (dotted curves) goes through a maximum for $\omega_0\tau_{CB}$ of the order unity. In a ^{139}La ($I = 7/2$) relaxation study of albumin solutions (7) the expression for the first-order longitudinal relaxation rate $\langle R_1 \rangle$ was used. For this case, with $\omega_0\tau_{CB} \approx 2$ and an estimated $Q \approx 100$, Figure 3 shows that the error is not less than 8%. Although, for given Q and $\omega_0\tau_{CB}$, the longitudinal decay is more nearly exponential (the dominating amplitude is closer to unity) than the transverse decay, it is seen that the first-order expressions may be less accurate in the longitudinal (dotted curves) than in the transverse (dashed curves) case. This is because the minor components are associated with larger relaxation rates in the longitudinal case.

When the apparent transverse relaxation rate is obtained from the linewidth



FIGS. 1-3. The ratio of the first-order relaxation rate $\langle R_\alpha \rangle$, given by Eq. [19], and the apparent rates R_1^{*e} (dotted curves), R_2^{*e} (dashed curves), or R_2^{*a} (solid curves), for indicated spin I . The dimensionless parameters are Q , which is defined by Eq. [21], and $\omega_0 \tau_{CB}$, the value of which appears beside each curve.

(solid curves) the accuracy of the approximation deteriorates, particularly for $I = 3/2$, because the slow components are weighted heavier in a linewidth measurement than in a Carr-Purcell R_2 measurement. Large differences between R_2^{*a}

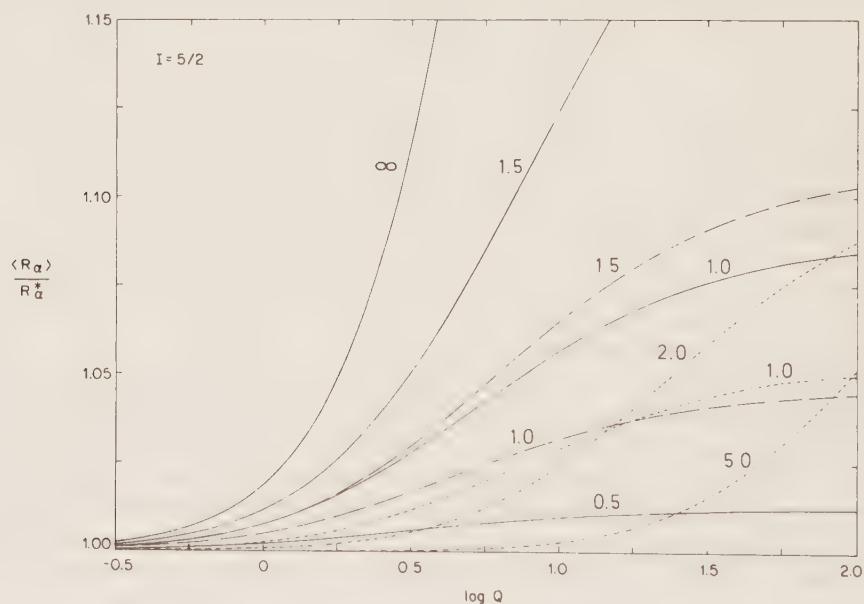


FIGURE 2

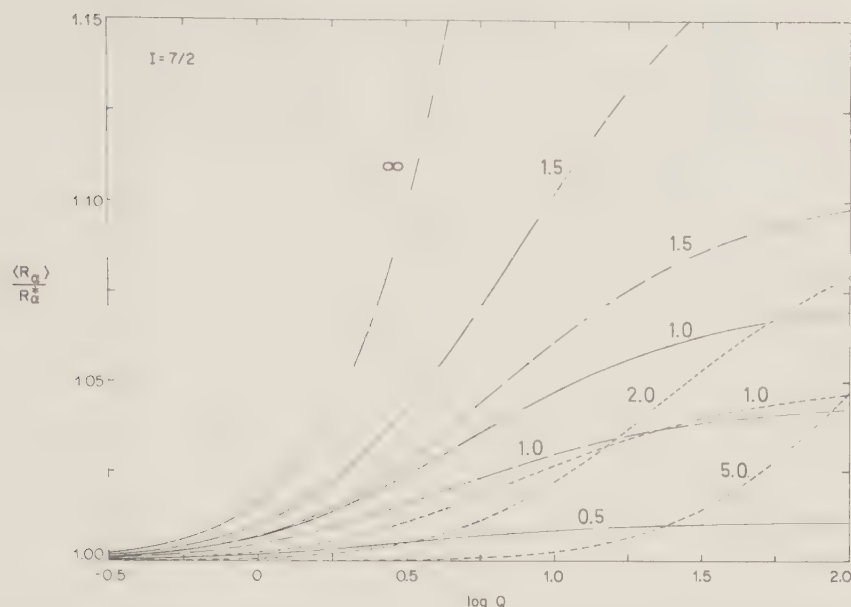


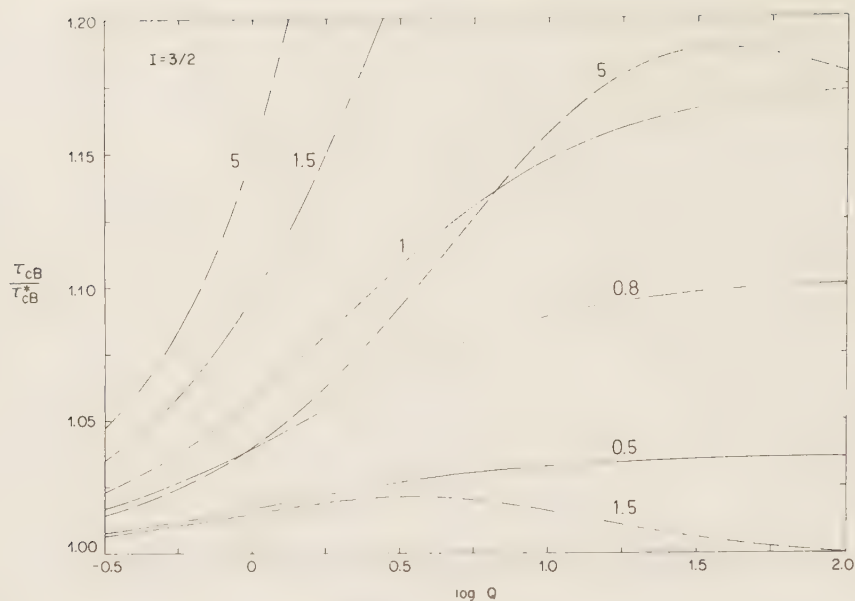
FIGURE 3

and R_2^{*e} have been observed for ^{23}Na ($I = 3/2$) in polyelectrolyte solutions (15). In electron spin resonance, it is customary to obtain R_2^* from the peak-to-peak distance in the derivative spectrum. The influence of the slowest component is then even greater. In fact, R_2^* measured in this way is nearly equal to the slowest component; e.g., for $I = 5/2$ the difference never exceeds 12%. This fact has been utilized in an ESR study of Fe^{3+} ($S = 5/2$) solutions (5).

For a given ratio $\langle R_2 \rangle / R_2^{*a}$, the deviation from Lorentzian lineshape becomes less pronounced with increasing spin I . It is doubtful whether, within the range of Figs. 1–3 ($\leq 15\%$ error), the slight ($\leq 10\%$) increase in amplitude in the wings of the absorption curve can be detected, even for $I = 3/2$. Moreover, within this range of error, the standard deviation of the exponential fits for determination of R_1^{*e} or R_2^{*e} is too small ($\leq 2\%$) to serve as an indicator of multiexponentiality. In the absence of reliable estimates of Q and $\omega_0\tau_{\text{CB}}$, the first-order expressions [14] should therefore be applied with caution.

The correlation time τ_{CB} for the B state may be obtained from the dispersion of either the longitudinal or the transverse relaxation rate. More commonly, however, τ_{CB} is calculated from the ratio of excess longitudinal and transverse rates at a single frequency. Since the ratio $\langle R_\alpha \rangle / R_\alpha^*$ is larger than one for the longitudinal as well as for the transverse rate, one would expect a cancellation effect in the error when evaluating τ_{CB} by this latter method. That this is indeed the case is shown in Figs. 4–6. Again, the accuracy is seen to improve dramatically in going from $I = 3/2$ to $5/2$. However, if R_2^* is obtained from a Carr–Purcell sequence (exponential fit) the accuracy is roughly independent of I . In agreement with previous calculations for $I = 3/2$ (24), Fig. 4 shows that, in this case, the error is negligible for $\omega_0\tau_{\text{CB}} \leq 1.5$.

The inherent anisotropy of the macromolecule–solvent interfacial region often



FIGS. 4-6. The ratio of the actual correlation time τ_{cB} and the apparent correlation time, τ_{cB}^* , obtained by equating the first-order relaxation rates with the corresponding apparent rates: R_1^{*e} and R_2^{*e} (dashed curves) or R_1^{*a} and R_2^{*a} (solid curves), for indicated spin I . The dimensionless parameters are Q , which is defined by Eq. [21], and $\omega_0\tau_{cB}$, the value of which appears beside each curve.

makes it convenient to regard the averaging of the quadrupole interaction as a two-step process: a fast local, slightly anisotropic reorientation and a slower, more extensive motion (25). If the local motion is sufficiently rapid (extreme narrowing)

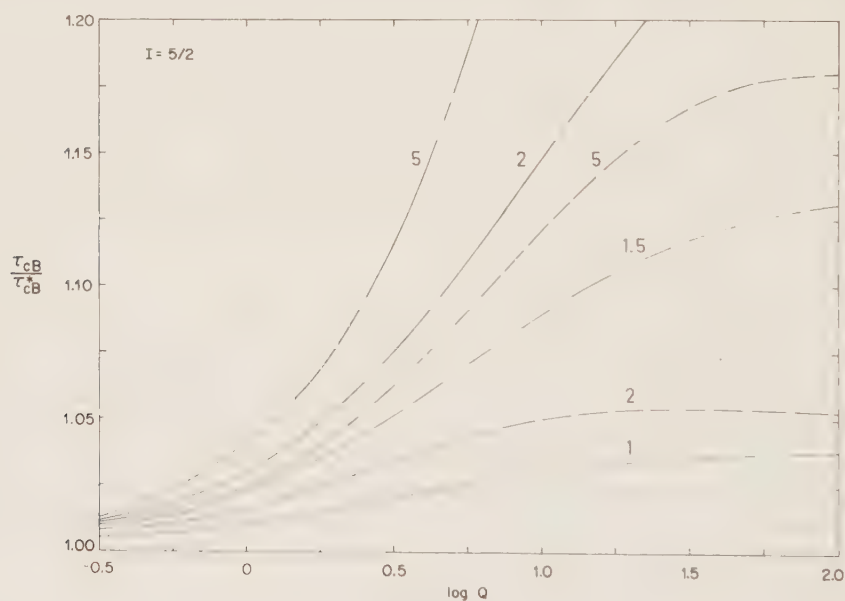


FIGURE 5

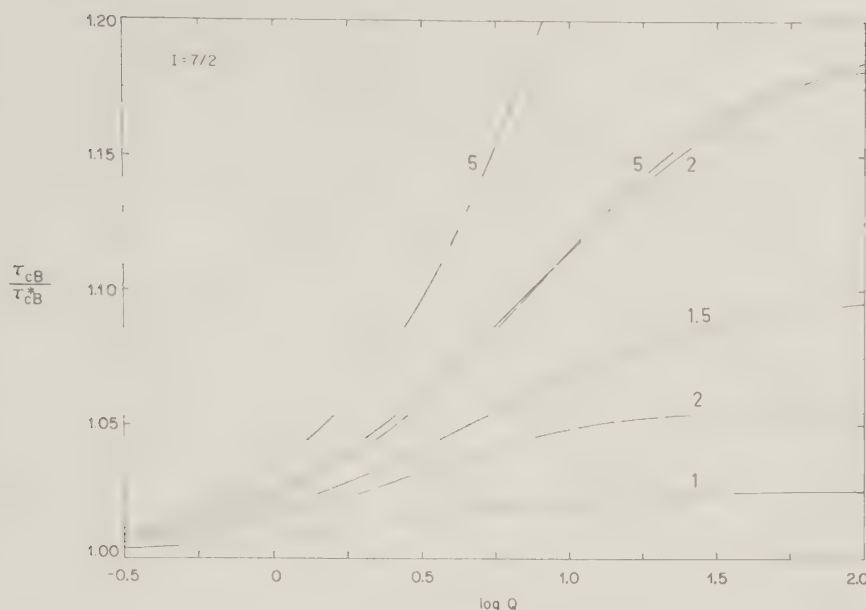


FIGURE 6

it will not contribute to the multiexponentiality, whereas for the slow motion the quadrupole coupling constant should, under certain conditions (25), be multiplied by an anisotropy factor A , the magnitude of which usually lies in the range 0.01 to 0.1. Thus by multiplying Q , as given by Eq. [21], by a factor A^2 , one obtains from Figs. 1–3 upper limits, corresponding to negligible contribution to the relaxation from the fast local motion, to the error appropriate for this model.

CONCLUSIONS

The perturbation treatment shows that the relaxation behavior is well described as a simple exponential decay with a rate given by Eq. [14], provided that the effective spectral density is only weakly frequency dependent. Calculations pertaining to a fast-exchange two-state model show that, for $I = 5/2$ and $7/2$, the first-order rates are accurate to within a few percent for Q values of the order of unity or less. For $I = 5/2$ and $7/2$ it seems, therefore, that the first-order expressions [14] will be useful in all cases, except, possibly, for large populations of species which are rigidly bound to large macromolecules.

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II

Interpretation of magnetic resonance data from water nuclei in heterogeneous systems

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Nuclear magnetic resonance (NMR) data from water nuclei (^1H , ^2H , and ^{17}O) can provide much information about the state of water in heterogeneous systems. In the present work, we present a theoretical framework for the interpretation of such data and discuss the implications of the theory. Due to the local anisotropy in heterogeneous systems, it is necessary to consider two components of water motion: a fast anisotropic reorientation superposed on a more extensive slow motion. On the basis of the experimentally verified assumption that these motions occur on different time scales, we develop a "two-step" model of relaxation, showing that both motions may give important contributions to the relaxation. We derive a simple expression for the relevant correlation function, valid for isotropic systems. Anisotropic systems are also treated, making use of a new symmetry theorem for time correlation functions. The proof of this theorem is given in an Appendix. The magnitudes of the water ^2H and ^{17}O quadrupole coupling constants are estimated to 0.222 and 6.67 MHz, respectively. Results of *ab initio* quantum chemical calculations are presented, demonstrating the insensitivity of the water ^{17}O field gradient to nearby ionic species. The possibilities and limitations of the NMR technique in answering the fundamental questions about water structure and dynamics in heterogeneous systems are discussed. We suggest a novel interpretation of the well-known invariance of the ratio of ^1H and ^2H splittings. Furthermore, we argue that the available NMR data are consistent with a short-ranged (≤ 2 molecular layers) perturbation of the water tumbling rate and anisotropy.

I. INTRODUCTION

The past few decades have seen a massive research effort directed towards an understanding of the state of water in heterogeneous systems. Prominent in this class of systems are aqueous solutions of macromolecules, in particular biopolymers, and large molecular aggregates, such as phospholipid bilayers and surfactant micelles. More complex systems, e.g., whole cells and tissues, have also been investigated. Furthermore, a variety of macroscopically anisotropic systems, such as oriented fibrous biopolymers, clays, and lyotropic liquid crystals, have been studied in great detail. (There are several recent reviews¹⁻⁸ that serve as introduction to the vast literature.) Despite the wealth of experimental data, no general consensus has emerged regarding some of the most fundamental characteristics of the water-surface interaction. In particular, the range of the surface-induced perturbation and the dynamics of perturbed water remain controversial issues.

A full understanding of the role played by the aqueous solvent in heterogeneous systems will require answers to questions of the following kind: How much water differs significantly from pure water and how does this amount depend on the molecular structure of the surface in terms of charged, polar, and hydrophobic groups as well as associated counterions? What is the shape of the orientational probability distribution of the perturbed water with respect to the surface, e.g., do well-defined hydration structures exist or does the surface induce only a small anisotropy in the average water orientation? What is the rate of perturbed water reorientation? How long time does an average water molecule spend in the perturbed region before it diffuses away into the bulk?

In addition, there are of course questions of a more specific nature relating to, for instance, biological function.

The experimental technique that is best suited to provide answers to these questions, in particular those concerned with dynamic aspects, is nuclear magnetic resonance (NMR). Of the three magnetic water nuclei, the proton, the deuteron, and oxygen-17, the former two have been utilized extensively, whereas relatively few ^{17}O studies have been reported. However, we expect water ^{17}O NMR to play an increasingly important role in future work, since this nucleus is not subject to complications such as cross-relaxation involving nonwater protons^{9,10} or chemical exchange mediated contributions from nonwater nuclei^{11,12} and is generally a more sensitive probe of water dynamics.

Nuclei with spin $I > \frac{1}{2}$ possess electric quadrupole moments and their NMR behavior is usually dominated by the interaction of the nuclear quadrupole with the electric field gradient at the nucleus. This is the case for ^2H ($I=1$) and ^{17}O ($I=5/2$). Through the observed relaxation rates and, for anisotropic systems, the splitting of the resonance line, the NMR experiment can give information about the anisotropy and rate of molecular motions through their modulation of the quadrupolar interaction. The main purpose of the present work is to provide a theoretical framework for the interpretation of quadrupolar relaxation rates and splittings for water ^2H and ^{17}O nuclei in heterogeneous systems. With slight modifications, the treatment is applicable also to the intramolecular dipole-dipole interaction observed in ^1H NMR.

The theoretical development is based on a model for the water motion, which has been found to be consistent with recent ^{17}O data obtained from aqueous solutions of proteins,¹³ linear polyelectrolytes,¹⁴ and surfactant micelles.¹⁵ The central feature of this model is the

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treatment of the averaging of the anisotropic quadrupolar interaction as a two-step process: a local, slightly anisotropic, reorientation superposed on a much slower motion, e.g., macromolecular reorientation or translational diffusion of water molecules between different environments.

The theory of quadrupolar relaxation and splittings in heterogeneous systems has previously been developed by Wennerström *et al.*,¹⁶ with particular reference to ionic nuclei, on the basis of the same dynamic model. The present derivation of the time correlation functions for the two-step model closely follows the previous work, but is somewhat more explicit and avoids the assumption of cylindrically symmetric field gradient, which is not valid for ^{17}O in water. It should also be mentioned that similar, but more specific, treatments have been presented¹⁷⁻²² in connection with ^2H relaxation studies of deuterated lipid bilayers and liquid crystals. The NMR behavior of water nuclei in heterogeneous systems has recently been discussed by Walmsley and Shporer²³; however, they did not consider the contribution to the relaxation from the fast, local motion. Furthermore, as will be discussed below, our conclusions are at variance with several other points in their paper.

In Sec. II we discuss the orientational probability distribution for the water molecule and its relation to the experimentally accessible order parameters. The field gradient tensors for ^2H and ^{17}O in water are then considered in some detail and values pertaining to liquid water are deduced from a combination of dielectric and NMR data. The insensitivity of the ^{17}O field gradient to the presence of nearby charges is demonstrated by results from *ab initio* quantum chemical calculations. The next three sections contain detailed derivations of expressions for line splittings and relaxation rates within the two-step model. Then follows a discussion of the possibilities and limitations of the NMR technique in providing structural and dynamic information about water in heterogeneous systems. In particular, we advance a novel interpretation of NMR data from multinuclear studies and address the questions of the range of the surface-induced perturbation and the separation of the contributions to the relaxation rates from the fast and slow motions. Relaxation in anisotropic systems is treated in more detail in Appendix A, using a general symmetry theorem for time correlation functions. The proof of this theorem is presented in Appendix B.

II. THE ORIENTATIONAL PROBABILITY DISTRIBUTION

The anisotropic interaction of water molecules with the surface of a macromolecule or a molecular aggregate constitutes a motional constraint on the otherwise isotropic water reorientation. The effect of this constraint may be quantified in terms of the probability distribution $P(\Omega)$ for the Eulerian angles Ω specifying the transformation between one coordinate system which is fixed in the (rigid) water molecule and another which is associated with the (rigid) surface. Following Zannoni, whose lucid account²⁴ of orientational probability functions in anisotropic systems provides the background for

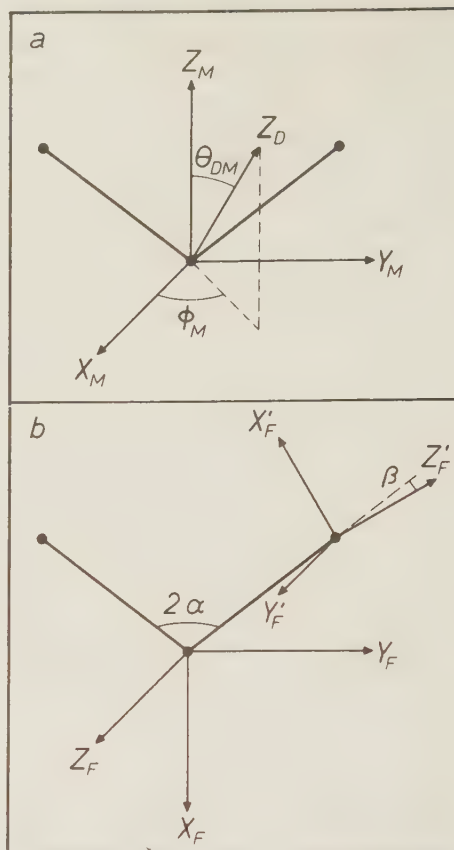


FIG. 1. Molecular (M) and director (D) coordinate systems (a), and principal axes systems (F) for the electric field gradient tensor at a deuterium nucleus (primed) and at the oxygen nucleus in the water molecule (b). The water nuclei lie in the plane of the paper, as do all coordinate axes except x_M , y'_F , and z_F , which are perpendicular to the plane, and z_D .

this section, we expand $P(\Omega)$ in a basis of Wigner rotation matrices²⁵

$$P(\Omega) = \sum_{l=0}^{\infty} \sum_{m=-l}^l \sum_{m'=-l}^l c_{m',m}^l D_{m',m}^{l*}(\Omega). \quad (1)$$

Multiplying both sides by $D_{m',m}^l(\Omega)$ and integrating over the angles we find

$$c_{m',m}^l = \left(\frac{2l+1}{8\pi^2} \right) \int d\Omega P(\Omega) D_{m',m}^l(\Omega) \equiv \left(\frac{2l+1}{8\pi^2} \right) \langle D_{m',m}^l(\Omega) \rangle, \quad (2)$$

because of the orthogonality of the Wigner rotation matrices.

The expansion (1) may be simplified by exploiting the symmetry of the constraint and of the water molecule. This is done by applying the appropriate symmetry operator R , which leaves $P(\Omega)$ unchanged, to Eq. (2)

$$\langle D_{m',m}^l(\Omega) \rangle = \int d\Omega P(\Omega) \langle lm' | RD(\Omega) | lm \rangle, \quad (3)$$

where the $|lm\rangle$ are the angular momentum eigenvectors. With the convention for the Eulerian angles used here, constraint symmetry operators should be applied from the left and molecular symmetry operators from the right.

As shown in Fig. 1(a), we choose a molecular coor-

dinate system (M) with z direction along the C_2 axis. In the surface coordinate system (D), the z axis, which will be referred to as the (local) director, is perpendicular to the surface. It is often reasonable to assume that, on the average, there is at least threefold symmetry around the director, i.e., that $P(\Omega_{DM})$ is invariant to the symmetry operator $C_3(z_D) = D(2\pi/3, 0, 0) = \exp(-i2\pi/3L_z)$, L_z being an angular momentum operator. According to Eq. (3), then

$$\langle D_{m'm}^l(\Omega_{DM}) \rangle = \exp(-im'2\pi/3) \langle D_{m'm}^l(\Omega_{DM}) \rangle, \quad (4)$$

which requires that $m' = 0$ for $l \leq 2$.

The C_{2v} symmetry of the water molecule demands that $P(\Omega_{DM})$ be invariant to the symmetry operators $C_2(z_M) = D(0, 0, \pi) = \exp(-i\pi L_z)$ and $\sigma(y_M z_M) = IC_2(x_M) = I \times \exp(-i\pi L_x)$, I being the inversion operator. According to Eq. (3), then

$$\langle D_{m'm}^l(\Omega_{DM}) \rangle = (-1)^m \langle D_{m'm}^l(\Omega_{DM}) \rangle, \quad (5)$$

which requires m to be even, and

$$\langle D_{m'm}^l(\Omega_{DM}) \rangle = \langle D_{m',-m}^l(\Omega_{DM}) \rangle, \quad (6)$$

which implies that $\langle D_{m'm}^l(\Omega_{DM}) \rangle$ depends only on the absolute value $|m|$.

Using the symmetry requirements (4)–(6) and the relation $D_{m'm}^{l*}(\Omega) = (-1)^{m'-m} D_{-m',-m}^l(\Omega)$, we find that the expansion (1), including terms up to $l=2$, reduces to

$$P(\Omega_{DM}) = \sum_{l=0}^2 \sum_{m=0}^{l/2} \left(\frac{2l+1}{8\pi^2} \right) S_{2m}^l \operatorname{Re} D_{0,2m}^l(\Omega_{DM}) + \dots, \quad (7)$$

where Re denotes the real part of a complex quantity and where $[l/2]$ is the greatest integer contained in $l/2$.

For $l \geq 3$ there will be terms with two nonzero subscripts, but only the $l=2$ contribution will be needed in the following. In Eq. (7) we have introduced the order parameters, which, for $l \leq 2$, are defined by

$$S_m^l \equiv (2 - \delta_{m0}) \operatorname{Re} \langle D_{0m}^l(\Omega_{DM}) \rangle. \quad (8)$$

The l th rank order parameters can be experimentally determined from properties that depend on interactions involving l th rank tensorial quantities. The relevant interactions in NMR studies of water nuclei are the magnetic dipole–dipole and the electric quadrupole interactions, both of which are described by second rank tensors. Consequently it is not possible to obtain, from NMR data alone, the complete orientational probability distribution $P(\Omega_{DM})$; usually, only the two second rank order parameters S_0^2 and S_2^2 can be extracted. Since the convergence of the expansion (7) may be very slow, it is thus clear that one cannot, solely on the basis of NMR data, obtain unique information about preferred water orientations. In other words, one cannot separately deduce the *locations* of minima on the surface of the potential of mean torque as well as their *depths*. This fact has not always been fully appreciated. On the other hand, any $P(\Omega_{DM})$ derived from microscopic models must, of course, be compatible with the experimental order parameters.

The explicit expressions for the two order parameters occurring in the NMR theory to be discussed are

$$S_0^2 = \langle D_{00}^2(\Omega_{DM}) \rangle = \frac{1}{2} (3 \langle \cos^2 \theta_{DM} \rangle - 1) = S_{zz}, \quad (9a)$$

$$S_2^2 = \langle D_{02}^2(\Omega_{DM}) \rangle + \langle D_{0,-2}^2(\Omega_{DM}) \rangle = \frac{\sqrt{6}}{2} \langle \sin^2 \theta_{DM} \cos 2\phi_M \rangle = \frac{2}{\sqrt{6}} (S_{xx} - S_{yy}), \quad (9b)$$

where we have also indicated the relation to elements of Saupe's traceless ordering tensor.²⁶

III. THE FIELD GRADIENT TENSORS

Quantitative interpretations of quadrupolar relaxation rates and line splittings require accurate values for the parameters describing the interaction of the nuclear quadrupole tensor with the electric field gradient tensor at the position of the nucleus. These parameters are conventionally taken as the quadrupole coupling constant χ and the asymmetry parameter η , defined by²⁷

$$\chi \equiv \frac{|eQ V_{zz}^F|}{h}, \quad (10)$$

$$\eta \equiv \frac{V_{xx}^F - V_{yy}^F}{V_{zz}^F}, \quad (11)$$

where h is Planck's constant, eQ is the (scalar) nuclear quadrupole moment, and the V_{ii}^F are the second partial derivatives, with respect to the field gradient principal axes (F), of the electric potential at the nucleus. The (dextral) principal axes are labeled so that $|V_{zz}^F| \geq |V_{xx}^F| \geq |V_{yy}^F|$, thereby restricting η to the range $[0, 1]$.

The orientation of the principal axes system F relative to the molecular geometry is of importance when the molecular motion modulating the quadrupole interaction is anisotropic. If this relation is known for several nonequivalent nuclei residing in the same molecule it may be possible to determine the components of the diffusion tensor for asymmetric top molecules²⁸ or for molecules in which internal rotations occur.²⁹ In heterogeneous systems, where the molecular motion is subject to *external* constraints, such knowledge, as we shall see, makes it possible to extract the order parameters S_0^2 and S_2^2 from the residual anisotropy of the quadrupolar interaction.

The orientations of the principal axes systems for the field gradient tensor at the position of the ^{17}O and a ^2H nucleus in the water molecule are shown in Fig. 1(b). These orientations have been deduced from beam-maser spectroscopic studies of the hyperfine structure of the $2_2 \rightarrow 2_1$ rotational transition of HD^{17}O in the gas phase³⁰ and from molecular orbital calculations on the isolated water molecule,^{31–34} on water oligomers,³⁵ and on several water–ion complexes (see below). Thus, we may safely assume that these are the orientations appropriate for liquid water in the bulk region as well as in the hydration region.

In spite of this unanimous evidence, other orientations for the ^{17}O principal axes have been used in several recent papers. The discrepancy may stem from an early microwave spectroscopic study,³⁶ which since has been shown to be in error.³⁰ It should also be stressed that the frequently cited ^{17}O NMR study by Spiess *et al.*³⁷ did not uniquely identify the y_F and z_F axes. This was clearly pointed out by the authors. In two recent stud-

TABLE I. Dielectric and quadrupolar data for water at 300.0 K.

Species	$\tau_{\text{die1}}(\text{ps})$	ϵ_r	ϵ_∞	$\tau_c(\text{ps})$	$R(\text{s}^{-1})$	$\chi(1+\frac{1}{3}\eta^2)^{1/2}$ (MHz)	η	χ (MHz)
^{17}O in H_2O	7.79 ^a	77.85 ^a	4.21 ^a	2.40	131.0 ^c	7.58	0.93	6.68
^{17}O in D_2O	10.03 ^b	77.23 ^b	4.0 ^b	3.10	167.4 ^c	7.55	0.93	6.65
^2H in D_2O	10.03 ^b	77.23 ^b	4.0 ^b	3.10	2.28 ^d	0.223	0.11	0.222

^aFrom a computer fit to data from seven studies reviewed in Ref. 47.^bFrom Ref. 48.^cFrom measurements in this laboratory on different samples using linewidth, CPMG, and inversion recovery data obtained on three spectrometers. Estimated uncertainty $\pm 2 \text{ s}^{-1}$.^dFrom Ref. 44.

ies^{38,39} of ^2H and ^{17}O splittings, the y_F and z_F axes as well as the x'_F and y'_F axes were interchanged. However, this did not affect the conclusions of the work, since only the idealized case with $\eta(^2\text{H})=0$ and $\eta(^{17}\text{O})=1$ was considered. On the other hand, in the comparison of water ^1H , ^2H , and ^{17}O NMR data by Walmsley and Shporer,²³ the interchange of the y_F and z_F axes has important consequences. In fact, if the correct axes orientations had been used the ^{17}O curve in Fig. 2 of their paper would have been displaced to the left sufficiently to invalidate their main conclusion.

The quadrupole coupling constants and the asymmetry parameters can be determined for the solid phase by NMR or NQR and for the gas phase by microwave spectroscopy. Since the molecular charge distribution is not expected to vary much between the liquid and solid states, the values of χ and η in liquid water should be nearly the same as those found in ice Ih. This assumption may be tested by calculating χ from the relaxation rates R , observed in liquid water, according to⁴⁰

$$R = \frac{3\pi^2}{10} \frac{2I+3}{I^2(2I-1)} \chi^2 \left(1 + \frac{\eta^2}{3}\right) \tau_c, \quad (12)$$

provided that an independent estimate of the correlation time τ_c is available. Anticipating the result of the calculation, we will use η values from measurements on ice Ih: $\eta(^2\text{H})=0.11$ (Refs. 41 and 42) and $\eta(^{17}\text{O})=0.93$. There is no significant difference between the value⁴³ 0.925 ± 0.02 for H_2^{17}O and the value³⁷ 0.935 ± 0.01 for D_2^{17}O . It should also be noted that the calculation of χ is not very sensitive to the value of η .

From the temperature and pressure dependence of the ^2H and ^{17}O relaxation rates it has been concluded that, in pure liquid water, the molecular reorientation can be described as an isotropic rotational diffusion process.^{44,45,51} The correlation time τ_c in Eq. (12) is then related to the macroscopic dielectric relaxation time τ_{die1} through⁴⁶

$$\tau_c = \frac{1}{3} f(\epsilon_r, \epsilon_\infty) \tau_{\text{die1}}, \quad (13)$$

where $f(\epsilon_r, \epsilon_\infty)$ is a correction factor relating the phenomenological quantity τ_{die1} to an average microscopic relaxation time. This correction is a function of the static and high-frequency relative permittivities ϵ_r and ϵ_∞ . The frequently used Glarum-Cole factor has recently been shown to be inaccurate⁴⁶; the improved cor-

rection factor is unity in the limit $\epsilon_r \gg \epsilon_\infty$, where the Glarum-Cole factor is $\frac{2}{3}$. However, a small correction for the distribution of microscopic relaxation times should be applied according to⁴⁶

$$f(\kappa) = \kappa^{-(2\kappa+1)^{-1}}, \quad (14)$$

where $\kappa \equiv \epsilon_r/\epsilon_\infty$.

Using Eqs. (12)–(14) and the data, for 300.0 K, given in Table I, we obtain $\chi(^2\text{H})=0.222$ MHz and $\chi(^{17}\text{O})=6.67$ MHz (no significant H/D isotope effect), in striking agreement with the experimental results for ice Ih: $\chi(^2\text{H})=0.214$ MHz^{41,42} and $\chi(^{17}\text{O})=6.52$ MHz⁴³ (H_2^{17}O), 6.66 MHz³⁷ (D_2^{17}O). It is thus plausible that also the η values are the same for liquid water and ice Ih. Previous estimates of the χ values for liquid water by combination of magnetic and dielectric relaxation data are either based on inaccurate ^{17}O relaxation rates^{49,50} or on the questionable Glarum-Cole correction.^{44,45} Our result for $\chi(^2\text{H})$ agrees well with the value 0.214 ± 0.012 MHz obtained by Lang and Lüdemann⁵¹ from the deuteron T_1 minimum at 192 K and 225 MPa in supercooled liquid D_2O . (No significant temperature dependence has been found in the quadrupole coupling constants for liquid water.^{44,50})

A question of great concern in the interpretation of water NMR data from heterogeneous systems is whether the field gradients are of purely intramolecular origin. It is thus conceivable that in water molecules associated with, for instance, charged surface groups, the field gradient tensors at the water nuclei are significantly perturbed as compared to the pure liquid. In order to estimate the magnitude of this perturbation, *ab initio* quantum chemical calculations of the water ^{17}O field gradient tensor for a large number of configurations of the systems $\text{H}_2\text{O}-\text{Li}^+$, $\text{H}_2\text{O}-\text{Na}^+$, and $\text{H}_2\text{O}-\text{Cl}^-$ were performed by Engström of this laboratory. The calculations were done with the MO-LCAO-SCF program⁵² MOLECULE, using basis sets (with minor modifications) from the work of Clementi *et al.*⁵³ For the isolated water molecule, this basis set yielded $V_{xx}^F=1.9287$, $V_{yy}^F=-1.7354$, $V_{zz}^F=-0.1933$ a.u. [principal axes as in Fig. 1(b)] and $\eta=0.800$, in close agreement with previous calculations.^{31–33}

The results of these calculations, for the more probable configurations (other configurations of comparable

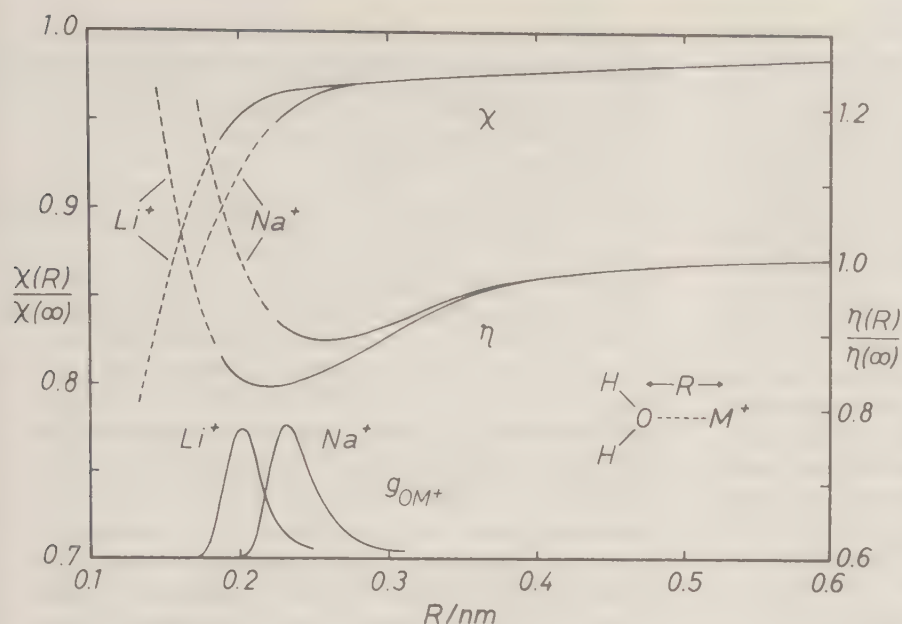


FIG. 2. The water ^{17}O quadrupole coupling constant χ and asymmetry parameter η , relative to their values for the isolated water molecule, vs the distance R between the oxygen and a lithium or a sodium ion approaching along a line bisecting the water lone pairs. The results were obtained from *ab initio* calculations as described in the text. The curves are dashed at R values shorter than the computed equilibrium distances. The radial distribution functions for the oxygen-ion distance, as obtained from Monte Carlo simulations with 50 water molecules at 300 K, are also shown.

energy gave similar results), are displayed in Figs. 2 and 3. These figures show the ^{17}O -ion distance dependence of χ and η and, for one configuration of lower than C_{2v} symmetry, of the principal axes orientation, relative to the values for the isolated water molecule. The dashed portion of each curve corresponds to oxygen-ion separations less than the equilibrium distance (deduced from the total energy minimum) for the indicated configuration. In the lower part of each figure, we have inserted the oxygen-ion radial distribution functions (averages over all configurations). These were obtained from Monte Carlo simulations⁵⁴ with 50 water molecules at 300 K, using potentials derived from the same basis sets⁵³ as were used for the field gradient calculations.

It is seen that the electrostatic perturbation is rather small, particularly for the cations. As the ion ap-

proaches to within the equilibrium separation, exchange repulsion leads to larger effects on the field gradient, but also makes the radial distribution functions decay rapidly. Within the full range of the calculated curves, the field gradient principal axes system conforms to Fig. 1(b), with the exception of configuration *a* in Fig. 3, in which case the principal frame is slightly rotated around the z_F axis ($\sim 10^\circ$ at the equilibrium distance).

For the cations, the ^{17}O quadrupole coupling constant χ is reduced by 5% at the radial distribution maximum and by 8% at the equilibrium distance for the selected configuration. The maximum changes in the asymmetry parameter η are 12% (Na^+) and 17% (Li^+). [Note that a 17% reduction in η propagates to a mere 7% reduction in the quantity $(1 + \eta^2/3)$, which appears in the expressions for the relaxation rates (cf. Sec. VI).] The chloride ion

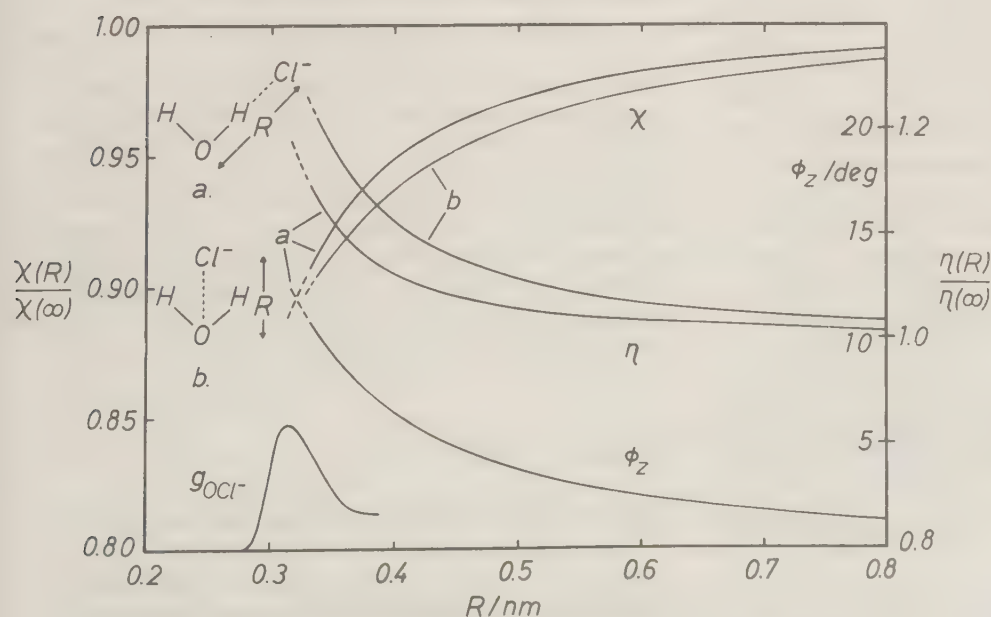


FIG. 3. The water ^{17}O quadrupole coupling constant χ and asymmetry parameter η , relative to their values for the isolated water molecule, vs the distance R between the oxygen and a chloride ion approaching along the extension of an O-H bond (a) or along a line bisecting the H-O-H angle (b). For case (a), the angle ϕ_z of rotation around the z_F axis [cf. Fig. 1(b)] of the principal axes system is also included. The results were obtained from *ab initio* calculations as described in the text. The curves are dashed at R values shorter than the computed equilibrium distances. The radial distribution function for the oxygen-chloride distance, as obtained from Monte Carlo simulations with 50 water molecules at 300 K, is also shown.

produces a slightly larger perturbation; at the equilibrium distance, χ is reduced by nearly 10%, while η is augmented by $\sim 20\%$.

In the NMR theory (see below), the first one or two water layers adjacent to a charged surface are usually treated as a single class, and average properties for these water molecules are deduced. Although a fraction of these water molecules may have somewhat ($\lesssim 10\%$) perturbed field gradients, the average $\chi(^{17}\text{O})$ will probably not differ significantly from its value in pure water. It should also be noted that, in the customary fast exchange case, the relaxation rates and splittings (see below) contain the product $P\chi$, where P is the fraction of water molecules in the "hydration region." In order to separate this product from other parameters (see below), one is often forced to estimate P from other experimental data, thereby introducing a much larger uncertainty than that associated with the field gradient.

IV. THE QUADRUPOLEAR HAMILTONIAN

The semiclassical Hamiltonian for the interaction of the nuclear quadrupole moment eQ with the electric field gradient at the nucleus may be written, in frequency units, as^{27,40}

$$H_Q(t) = \frac{eQ}{2I(2I-1)\hbar} \sum_m (-1)^m A_{-m} V_m(t). \quad (15)$$

Here and in the following, unless otherwise noted, all sums run from -2 to $+2$. I is the nuclear spin quantum number, the A_m are second rank irreducible spin tensor operators

$$A_0 = \frac{1}{\sqrt{6}} [3I_z^2 - I(I+1)], \quad (16a)$$

$$A_{\pm 1} = \mp \frac{1}{2} [I_z I_{\pm} + I_{\pm} I_z], \quad (16b)$$

$$A_{\pm 2} = \frac{1}{2} I_{\pm}^2, \quad (16c)$$

and the V_m are components of the second rank irreducible field gradient tensor

$$V_0 = \frac{1}{2} \sqrt{6} V_{zz}, \quad (17a)$$

$$V_{\pm 1} = \mp [V_{xz} \pm iV_{yz}], \quad (17b)$$

$$V_{\pm 2} = \frac{1}{2} [V_{xx} - V_{yy} \pm i2V_{xy}]. \quad (17c)$$

The scalar contraction in Eq. (15) may be evaluated in any coordinate system. The spin operators are most conveniently expressed in a laboratory-fixed frame (L), the z direction of which is defined by the external static magnetic field. The field gradient components, on the other hand, are more naturally expressed in the principal axes system (F) fixed at the nucleus in question

[Fig. 1(b)]. The transformation to this coordinate system can be effected with the aid of the second rank Wigner rotation matrix²⁵

$$\begin{aligned} V_m^L(t) &= \sum_{m'} D_{m',m}^2[\Omega_{FL}(t)] V_{m'}^F \\ &= \sum_{m'} (-1)^{m'-m} D_{-m,-m'}^2[\Omega_{LF}(t)] V_{m'}^F. \end{aligned} \quad (18)$$

The phase convention is according to Rose²⁵ and the Eulerian angles are $\Omega_{LF} = (\phi_L, \theta_{LF}, \phi_F)$. For the ^2H and ^{17}O water nuclei, it is an excellent approximation (cf. the previous section) to regard the field gradient as being generated exclusively by intramolecular charges. The components $V_{m'}^F$ are then constant and the time dependence is confined to the Eulerian angles $\Omega_{LF}(t)$ describing the molecular reorientation.

In order to describe the motion of water molecules in heterogeneous systems, it is convenient to introduce two additional coordinate systems: the director system (D), with its z axis perpendicular to the surface, and the molecular system (M), the z axis of which coincides with the water C_2 axis [Fig. 1(a)]. For the successive transformations $L \rightarrow D \rightarrow M \rightarrow F$ we find

$$\begin{aligned} V_m^L(t) &= \sum_{m'} \sum_{m''} \sum_{m'''} (-1)^{m'''-m} D_{-m,-m'}^2[\Omega_{LD}(t)] \\ &\quad \times D_{-m',-m''}^2[\Omega_{DM}(t)] D_{-m'',-m'''}^2(\Omega_{MF}) V_{m'''}^F. \end{aligned} \quad (19)$$

It will now be assumed that the motions giving rise to the time dependence in $\Omega_{LD}(t)$ and in $\Omega_{DM}(t)$, respectively, occur on so different time scales that Ω_{LD} remains essentially constant over periods of time sufficient for statistical averaging of Ω_{DM} . This assumption constitutes the basic feature of the two-step model. If, as in the preceding, we denote the averaging operation $\int d\Omega_{DM} \times P(\Omega_{DM})$ by angular brackets, but with the addition of the subscript DM to distinguish it from other averages to appear later, then

$$\begin{aligned} \langle D_{-m,-m'}^2[\Omega_{LD}(t)] D_{-m',-m''}^2[\Omega_{DM}(t)] \rangle_{DM} \\ = \delta_{m',0} D_{-m,0}^2[\Omega_{LD}(t)] \langle D_{0,-m''}^2(\Omega_{DM}) \rangle_{DM} \end{aligned} \quad (20)$$

because of the form (7) of $P(\Omega_{DM})$, which, it will be remembered, presupposes threefold symmetry around the director, and because of the orthogonality of the Wigner rotation matrices. The quadrupolar Hamiltonian (15) will now be divided into one part with slow time dependence (subscript s) and another with fast time dependence (subscript f), corresponding to the two steps of motional averaging of the quadrupolar interaction. Using Eqs. (19) and (20), we find

$$H_s(t) \equiv \langle H_Q(t) \rangle_{DM} = \frac{eQ}{2I(2I-1)\hbar} \sum_m \sum_{m'} \sum_{m''} A_m D_{m,0}^2[\Omega_{LD}(t)] \langle D_{0,-m''}^2(\Omega_{DM}) \rangle_{DM} D_{m'',m'''}^2(\Omega_{MF}) V_{m'''}^F, \quad (21)$$

$$\begin{aligned} H_f(t) \equiv H_Q(t) - \langle H_Q(t) \rangle_{DM} &= \frac{eQ}{2I(2I-1)\hbar} \sum_m \sum_{m'} \sum_{m''} \sum_{m'''} A_m D_{m,m'}^2(\Omega_{LD}) \{ D_{m',m''}^2[\Omega_{DM}(t)] - \delta_{m',0} \langle D_{0,-m''}^2(\Omega_{DM}) \rangle_{DM} \} \\ &\quad \times D_{m'',m'''}^2(\Omega_{MF}) V_{m'''}^F, \end{aligned} \quad (22)$$

where some minus signs have been eliminated by noting that the sums are symmetrical and that, according to Eq. (17), $V_{m'''}^F$ is independent of the sign of m''' and nonzero only for even m''' .

V. LINE SPLITTINGS

If the motion which modulates $\Omega_{LD}(t)$ is slow compared to the residual quadrupolar interaction $H_s(t)$, then the absorption line at the resonance frequency will be split into $2I$ lines. At ordinary magnetic field strengths, the quadrupolar interaction is very small compared to the Zeeman interaction and only the secular part of H_s , corresponding to $m=0$ in Eq. (21), has to be considered. Neglecting the time dependence in Ω_{LD} (see below), we then get the following nuclear spin Hamiltonian:

$$H_{sec} = -\nu_0 I_z + \frac{A\chi}{8I(2I-1)} \times (3 \cos^2 \theta_{LD} - 1) [3I_z^2 - I(I+1)], \quad (23)$$

where we have used Eqs. (10), (17), and (21) and defined

$$A \equiv (V_0^F)^{-1} \sum_m \sum_{m'} \langle D_{0m}^2(\Omega_{DM}) \rangle_{DM} D_{mm'}^2(\Omega_{MF}) V_{m'}^F. \quad (24)$$

This quantity is sometimes referred to simply as the order parameter, but since it depends, in general, not only on the true order parameters (9), but also on the molecular geometry and on the symmetry of the interaction tensor, we will call it the *residual (quadrupolar) anisotropy*. It is easily shown that A is confined to the range $[-1, 1]$ and that for isotropic motion, with $P(\Omega_{DM}) = 1/8\pi^2$, $A = 0$.

It is straightforward to show^{27,40} that, to first order in the quadrupolar perturbation, the Hamiltonian (23) corresponds to an NMR spectrum consisting of $2I$ lines of relative intensity $I(I+1) - m(m+1)$, with $m = -I, -I+1, \dots, I-1$, centered at ν_0 and equally spaced by the quadrupolar splitting

$$\Delta = \frac{3\chi}{4I(2I-1)} |(3 \cos^2 \theta_{LD} - 1)A|. \quad (25)$$

Since the dipole-dipole interaction has the same symmetry properties as the quadrupolar interaction, the dipolar splitting observed in ^1H NMR is also given by Eq. (25), but with the replacement $\chi/I(2I-1) \rightarrow (\mu_0/4\pi)\hbar\gamma^2/\pi r^3$, where $\mu_0/4\pi = 10^{-7} \text{ Vs(Am)}^{-1}$, $\gamma = 2.675 \times 10^8 \text{ rad (Ts)}^{-1}$, and, for the proton pair in H_2O , $r = 0.152 \text{ nm}$. Equation (24) is valid also for the residual dipolar anisotropy; then $m' = 0$ and the z_F axis is defined by the H-H vector.

Depending on the detailed molecular structure of the surface, there will be a more or less wide distribution of water sites characterized by different water-surface and water-water interactions. If the exchange of *water molecules* between such sites is fast compared to the difference in splitting, then the observed order parameters, entering the expression (24) for A , will be population weighted averages

$$S_m^2 = \sum_i P_i S_{mi}^2, \quad (26)$$

where P_i is the fraction of water molecules in the i th site. It should be borne in mind, that the order parameters for different sites may differ in sign, leading to a partial cancellation of terms in the sum (26) and consequently to a small observed residual anisotropy. The

averaging in Eq. (26) can result also from rapid exchange of *deuterons* between water molecules residing in different sites or with the surface. Thus the observed ^2H splitting may contain contributions from acidic surface groups.⁷²⁻⁷⁴ To account for the different ^2H field gradient in the surface groups, Eq. (26) should be replaced by $\chi|A| = |\sum_i P_i \chi_i A_i|$. Rapid *proton* exchange (with surface groups or among water molecules), on the other hand, always leads to complete elimination of the dipolar ^1H splitting.^{67,80}

Not only the local motion described by $\Omega_{DM}(t)$, but also motions producing a time dependence in Ω_{LD} , will reduce the quadrupolar splitting. This is the case in systems with nonplanar surfaces and a lateral water diffusion which is fast compared to the splitting. A simple and important example is that of oriented fibers or cylindrical aggregates. By performing the $L \rightarrow D$ transformation via a coordinate system, the z axis of which is defined by the (at least threefold) optical axis, it is straightforward to show¹⁶ that the splitting, in this case, is reduced by a factor $1/2$.

For a polycrystalline or powder sample, where all director orientations are equally probable, the observed spectrum is a superposition of spectra corresponding to all possible Ω_{LD} . This, of course, presupposes that water diffusion between domains with different orientations is slow compared to the difference in splitting; otherwise the splitting will collapse into a single line. Provided that the line width is small compared to the splitting, the powder splitting is given by Eq. (25) with $\theta_{LD} = \pi/2$, since this value predominates in an isotropic distribution.^{27,40}

VI. RELAXATION RATES IN ISOTROPIC SYSTEMS

The term *isotropic* is used here to denote the condition that the residual quadrupolar interaction is completely averaged out by the slow motion, represented by $\Omega_{LD}(t)$, during a period of time that is short compared to the inverse of that interaction. Thus, $P(\Omega_{LD}) = 1/8\pi^2$ is a necessary, although not sufficient, condition for a system to be isotropic in this sense; in addition, the condition on the rate of change of $\Omega_{LD}(t)$ must be satisfied. The longitudinal and transverse quadrupolar relaxation rates in isotropic systems are⁴⁰

$$R_1 = K[2J(\omega_0) + 8J(2\omega_0)], \quad (27a)$$

$$R_2 = K[3J(0) + 5J(\omega_0) + 2J(2\omega_0)], \quad (27b)$$

where

$$K \equiv \frac{1}{80} \frac{2I+3}{I^2(2I-1)} \left(\frac{eQ}{\hbar} \right)^2. \quad (27c)$$

The spectral densities $J(\omega)$ are Fourier transforms of the time correlation function $G(t)$ of the zeroth component of the irreducible field gradient tensor, expressed in the laboratory frame

$$J(\omega) \equiv \int_{-\infty}^{\infty} dt e^{-i\omega t} G(t), \quad (28)$$

$$G(t) \equiv \langle V_0^{L*}(0) V_0^L(t) \rangle_{LM}, \quad (29)$$

where the subscript LM indicates that the ensemble av-

erage involves Ω_{LD} as well as Ω_{DM} .

Water in heterogeneous systems is usually distributed over several environments, e.g., a perturbed region and a bulk region, characterized by different intrinsic relaxation rates and resonance frequencies. If, as seems to be the rule, the water molecules exchange rapidly relative to the relaxation rates and to the difference in resonance frequency, then the observed relaxation rates are population weighted averages^{55, 56}

$$R_\alpha = \sum_i P_i R_{\alpha i} \quad (\alpha = 1, 2). \quad (30)$$

The intrinsic relaxation rate for the bulk water in a heterogeneous system is, by definition, equal to the rate measured for a sample containing only the aqueous medium. Consequently, the problem is to relate the intrinsic relaxation rates for the *perturbed* water to the details of the molecular motion. The link between the relaxation rates and the microdynamics is provided by the time correlation function $G(t)$, the derivation of which is the main task in this section.

The expressions (27) are strictly valid only when the macroscopic magnetization decays exponentially. This is, in general, not true for ^{17}O with $I = 5/2$.⁴⁰ However, for most systems of interest, the effective spectral density $J(\omega) = \sum_i P_i J_i(\omega)$ is, at ordinary magnetic field strengths, only weakly frequency dependent. The decay is then very nearly exponential and the Eqs. (27) are excellent approximations.⁵⁷

We now turn to the derivation of an expression for the correlation function $G(t)$ valid for the two-step model,

in which a slow and a fast, slightly anisotropic, motion both contribute to the relaxation in a perturbed state. (In the following, we omit the state subscript i .) Using Eqs. (19) and (20), we can divide $V_0^L(t)$ into parts with slow and fast time dependence

$$[V_0^L(t)]_s = A V_0^F D_{00}^2[\Omega_{LD}(t)], \quad (31)$$

$$[V_0^L(t)]_f = \sum_m \sum_{m'} \sum_{m''} D_{0m}^2(\Omega_{LD}) \{ D_{mm'}^2[\Omega_{DM}(t)] - \delta_{m0} \langle D_{0m}^2(\Omega_{DM}) \rangle_{DM} \} D_{m'm''}^2(\Omega_{MF}) V_{m''}^F, \quad (32)$$

where, in Eq. (31), we have introduced the residual anisotropy A according to the definition (24).

In the two-step model, the fast and slow motions are assumed to occur on separated time scales. Consequently, these motions are *statistically independent*, i.e., there are no cross correlations and

$$G(t) = G_f(t) + G_s(t). \quad (33)$$

Equations (29) and (31) lead directly to

$$G_s(t) = (A V_0^F)^2 \langle D_{00}^{2*}[\Omega_{LD}(0)] D_{00}^2[\Omega_{LD}(t)] \rangle_{LD} = \frac{1}{5} (A V_0^F)^2 \tilde{G}_s(t), \quad (34)$$

where we have introduced the reduced correlation function

$$\tilde{G}(t) \equiv G(t)/G(0) \quad (35)$$

and made use of the orthogonality of the Wigner rotation matrices.

The derivation of $G_f(t)$ requires considerably more effort. From Eqs. (29) and (32) we find

$$G_f(t) = \sum_m \sum_{m'} \sum_{m''} \sum_{q'} \sum_{q''} \langle D_{0m}^{2*}(\Omega_{LD}) D_{0q}^2(\Omega_{LD}) \rangle_{LD} D_{m'm''}^{2*}(\Omega_{MF}) D_{q''q'}^2(\Omega_{MF}) \times V_{m''}^F V_{q'}^F \{ \langle D_{mm'}^{2*}[\Omega_{DM}(0)] D_{mq'}^2[\Omega_{DM}(t)] \rangle_{DM} - \delta_{m0} \delta_{q0} \langle D_{0m}^{2*}(\Omega_{DM}) \rangle_{DM} \langle D_{0q}^2(\Omega_{DM}) \rangle_{DM} \}, \quad (36)$$

where the symmetry requirement (4) has been used. In an isotropic system, $P(\Omega_{LD}) = 1/8\pi^2$, and Eq. (36) can be simplified by means of the orthogonality of the Wigner rotation matrices, to obtain

$$G_f(t) = \frac{1}{5} \sum_{m'} \sum_{m''} \sum_{q'} \sum_{q''} \{ D_{m'm''}^{2*}(\Omega_{MF}) D_{q''q'}^2(\Omega_{MF}) V_{m''}^F V_{q'}^F \sum_m \langle D_{mm'}^{2*}[\Omega_{DM}(0)] D_{mq'}^2[\Omega_{DM}(t)] \rangle_{DM} \} - \frac{1}{5} (A V_0^F)^2, \quad (37)$$

where definition (24) has been used.

To proceed, we will now make the assumption that the time dependence of the correlation function is the same for all values of m , m' , and q' , i.e., that

$$\langle D_{mm'}^{2*}[\Omega_{DM}(0)] D_{mq'}^2[\Omega_{DM}(t)] \rangle_{DM} = [\langle D_{mm'}^{2*}(\Omega_{DM}) D_{mq'}^2(\Omega_{DM}) \rangle_{DM} - \delta_{m0} \langle D_{0m}^{2*}(\Omega_{DM}) \rangle_{DM} \langle D_{0q'}^2(\Omega_{DM}) \rangle_{DM}] \tilde{G}_f(t) + \delta_{m0} \langle D_{0m}^{2*}(\Omega_{DM}) \rangle_{DM} \langle D_{mq'}^2(\Omega_{DM}) \rangle_{DM}. \quad (38)$$

This is a reasonable approximation if the fast motion is only slightly anisotropic. The anisotropy of the local environment is, in this approximation, explicitly accounted for solely through its effect on the *equilibrium* properties of the system, i.e., on the orientational distribution $P(\Omega_{DM})$. [This would also be the case if the fast motion were described by a strong collision model⁵⁸; Eq. (38), however, constitutes a less restrictive condition.]

Since the averages $\langle D_{mm'}^{2*}(\Omega_{DM}) \rangle_{DM}$ are nonzero for the *anisotropic* fast motion, we have, in Eq. (38), subtracted the residual part of the interaction, which is modulated by the slow motion. The reduced correlation function $\tilde{G}_f(t)$ thereby acquires the desired properties of being unity at $t=0$ and zero as $t \rightarrow \infty$. [The Kronecker deltas in Eq. (38) follow from the threefold symmetry according to Eq. (4).] Introduction of the approximation (38) into Eq. (37) now leads to

$$G_f(t) = \left\{ \frac{1}{5} \sum_{m'} \sum_{m''} \sum_{q'} \sum_{q''} [D_{m'm''}^{2*}(\Omega_{MF}) D_{q''q'}^2(\Omega_{MF}) V_{m''}^F V_{q'}^F \sum_m \langle D_{mm'}^{2*}(\Omega_{DM}) D_{mq'}^2(\Omega_{DM}) \rangle_{DM}] - \frac{1}{5} (A V_0^F)^2 \right\} \tilde{G}_f(t). \quad (39)$$

Using the product formula for D elements and the orthogonality relation for 3- j symbols,²⁵ we find that Eq. (39) reduces to

$$G_f(t) = \frac{1}{5} \left\{ \sum_m [(-1)^m V_m^F V_{-m}^F] - (A V_0^F)^2 \right\} \tilde{G}_f(t). \quad (40)$$

Finally, we sum over m , using definitions (11) and (17), to obtain

$$G_f(t) = \frac{1}{5} (V_0^F)^2 (1 + \frac{1}{3} \eta^2 - A^2) \tilde{G}_f(t). \quad (41)$$

Combination of Eqs. (33), (34), and (41) gives the complete correlation function

$$G(t) = \frac{3}{10} (V_{zz}^F)^2 \left[(1 + \frac{1}{3} \eta^2 - A^2) \tilde{G}_f(t) + A^2 \tilde{G}_s(t) \right]. \quad (42)$$

To summarize: This expression is valid for an isotropic system in which the quadrupolar interaction is partially averaged by a fast, slightly anisotropic, motion with at least threefold symmetry with respect to the local director, the residual anisotropy being averaged out by a much slower (although fast compared to the residual interaction) motion. If the fast motion were completely isotropic, i.e., if $P(\Omega_{DM}) = 1/8\pi^2$, then $A = 0$ and Eq. (42) reduces to the well-known isotropic result.⁴⁰ It may be noted that Eq. (42) is valid, apart from the constant in front of the square brackets, also for relaxation through intramolecular dipole-dipole interaction. (In that case, one should set $\eta = 0$.)

In certain cases, $\tilde{G}_s(t)$ may involve more than one correlation time. As an example, assume that the slow motion can be described as a rotational diffusion of a symmetric top. In order to find an explicit expression for $\tilde{G}_s(t)$ in terms of the two rotational diffusion coefficients, one would then perform the $L \rightarrow D$ transformation via the principal axes system (R) of the diffusion tensor, to obtain

$$\begin{aligned} \tilde{G}_s(t) = 5 \sum_m \langle D_{m0}^{2*}(\Omega_{RD}) D_{m0}^2(\Omega_{RD}) \rangle_{RD} \\ \times \langle D_{0m}^{2*}[\Omega_{LR}(0)] D_{0m}^2[\Omega_{LR}(t)] \rangle_{LR}. \end{aligned} \quad (43)$$

The correlation functions are obtained from the solution of the rotational diffusion equation,²⁸ while the averages over the local director orientation can be evaluated by purely geometrical considerations.

Another case of interest is when rotational as well as translational (chemical exchange) motions contribute to the slow time dependence. With an isotropic rotational correlation time τ_r and a mean lifetime τ_l for a water molecule in the perturbed state, the reduced correlation function is⁵⁶

$$\tilde{G}_s(t) = \exp \left[-|t| \left(\frac{1}{\tau_r} + \frac{1}{\tau_l} \right) \right]. \quad (44)$$

To obtain this result one has to neglect the finite probability that a water molecule, after leaving the perturbed state associated with a particular aggregate, returns to the same aggregate. (A correlation function which includes this effect may be derived using the kinetic theory of recombination processes.⁵⁹) Any τ_l determined from relaxation data using Eq. (44) should therefore be regarded as an apparent lifetime, which is longer than the true lifetime.

VII. RELAXATION RATES IN ANISOTROPIC SYSTEMS

In anisotropic systems, the $2I$ transitions between the perturbed Zeeman levels are nondegenerate and characterized by relaxation rates which differ from the isotropic result (27). Although much useful information can be gained by selectively stimulating individual transitions,^{58,60} the following discussion will be restricted to transverse relaxation rates R_2 obtained from linewidths. In order to derive expressions for these rates, one usually starts from the equation of motion⁶¹ for the spin density matrix elements $\chi_{mm'}$

$$\begin{aligned} \frac{d\chi_{mm'}(t)}{dt} = i(m - m')\omega_0 \chi_{mm'}(t) \\ + \sum_{n=-I}^I \sum_{n'=-I}^I R_{mm'nn'} \chi_{nn'}(t), \end{aligned} \quad (45)$$

where the elements $R_{mm'nn'}$ of the relaxation matrix involve spin operator matrix elements and spectral densities characterizing the fluctuating interaction.

If the linewidth is small relative to the splitting, the relaxation rate R_2 for each transition is given by a single element of the relaxation matrix⁵⁸

$$R_2(m \leftrightarrow m+1) = -R_{mm+1mm+1}. \quad (46)$$

From the general expression for the relaxation matrix,⁶¹ we find for the ^2H doublet

$$R_2(\pm 1 \leftrightarrow 0) = K[3J_0(0) + 3J_1(\omega_0) + 2J_2(2\omega_0)] \quad (47)$$

and for the ^{17}O quintet

$$R_2(-\frac{1}{2} \leftrightarrow \frac{1}{2}) = \frac{5}{18} K[8J_1(\omega_0) + 28J_2(2\omega_0)], \quad (48a)$$

$$R_2(\pm \frac{1}{2} \leftrightarrow \pm \frac{3}{2}) = \frac{5}{18} K[3J_0(0) + 18J_1(\omega_0) + 23J_2(2\omega_0)], \quad (48b)$$

$$R_2(\pm \frac{3}{2} \leftrightarrow \pm \frac{5}{2}) = \frac{5}{18} K[12J_0(0) + 24J_1(\omega_0) + 14J_2(2\omega_0)], \quad (48c)$$

where the constant K is given by Eq. (27c) and the spectral densities $J_k(\omega)$ are Fourier transforms of correlation functions

$$G_k(t) \equiv \langle V_k^{L*}(0) V_k^L(t) \rangle_{LM}. \quad (49)$$

It may be noted that Eq. (47), with appropriately defined K , applies also to intramolecular dipole-dipole relaxation involving equivalent spins.

Expressions for the correlation functions (49) within the two-step model may be derived along the same lines as in the preceding section. However, without additional approximations, the final result is considerably more complicated than Eq. (42). In particular, the correlation functions, and thus also the relaxation rates, depend on the director orientation Ω_{LD} . Moreover, the correlation functions involve, not only second rank, but also fourth rank D elements. These complications are further discussed in Appendix A, where we derive expressions for the correlation functions $G_k(t)$ for the anisotropic case. This derivation makes use of a general symmetry theorem for time correlation functions, which to our knowledge has not previously appeared in the literature. We therefore supply a proof of the theorem in Appendix B.

In cases where the time dependence in Ω_{LD} may be neglected and where the fast motion is rapid compared to the resonance frequency ("extreme narrowing" conditions) and only slightly anisotropic, a reasonable first approximation is

$$J_f = \frac{3}{5}(V_{zz}^F)^2(1 + \frac{1}{3}\eta^2 - A^2)\tau_f, \quad (50)$$

where an exponential form for $\tilde{G}_f(t)$ has been assumed. Within this approximation, Eq. (48) predicts that the ^{17}O satellite linewidths, relative to the central line, should be 1.22 and 1.39. These figures may be compared to the spectrum for a macroscopically aligned lyotropic mesophase, reported by Niederberger and Tricot,³⁸ with relative linewidths 1.21 and 1.45.

Another possible source of time dependence in the quadrupolar interaction is a chemical exchange between states characterized by different residual anisotropies, i.e., different effective quadrupolar couplings. For a two-state case, where the fast reorientational motion is rapid compared to the exchange rate, one finds^{16,56}

$$J_{\text{ex}}^{\text{ex}}(\omega) = 3P(1-P)[A V_{zz}^F d_{k0}^2(\theta_{LD})]^2 \frac{\tau_{\text{ex}}}{1 + (\omega\tau_{\text{ex}})^2}, \quad (51)$$

where P is the fraction of nuclei in the "bound" state with anisotropy A . (The "free" state is taken to be isotropic, i.e., $A=0$ in that state.) The $d_{k0}^2(\theta_{LD})$ are reduced second rank Wigner rotation matrix elements²⁵ and τ_{ex} is the exchange time, which is related to the mean lifetime in the bound state through $\tau_{\text{ex}} = (1-P)\tau_1$. An expression equivalent to Eq. (51) has recently been derived by Burnell *et al.*⁶²

For a polycrystalline sample, where all values of Ω_{LD} are represented, a distribution of relaxation rates will be observed.¹⁶ However, if the anisotropy is small, the distribution will be correspondingly narrow. Because of the frequency distribution of the satellites, only the central linewidth is directly related to a relaxation rate. Additional information can, however, be obtained using selective radio-frequency pulses.^{58,60} In polycrystalline samples, water diffusion between microcrystallites with different orientations (Ω_{LD}) may also contribute to the relaxation. This case has been treated by Woessner.⁶³

VIII. ORDER PARAMETERS FROM MULTINUCLEAR STUDIES

Information about the water orientational probability distribution $P(\Omega_{DM})$ is contained in the residual anisotropy A , which is most directly determined from line splittings in anisotropic systems. From Eqs. (6), (9), (11), (17), and (24), we find

$$A = \text{Re} \left[D_{00}^2(\Omega_{MF}) + \frac{2\eta}{\sqrt{6}} D_{02}^2(\Omega_{MF}) \right] S_0^2 + \text{Re} \left\{ D_{20}^2(\Omega_{MF}) + \frac{\eta}{\sqrt{6}} [D_{22}^2(\Omega_{MF}) + D_{2-2}^2(\Omega_{MF})] \right\} S_2^2. \quad (52)$$

According to Fig. 1, $\Omega_{MF}(^1\text{H}) = (\pi/2, \pi/2, 0)$ and $\Omega_{MF}(^{17}\text{O}) = (0, \pi/2, 0)$. Experimental data^{30,64} and computational results³¹⁻³⁴ for the angle β between the z'_F axis and the O-D bond are scattered around zero in the range $\pm 3^\circ$. It should therefore be an excellent approximation to set

$\beta=0$, whereby Fig. 1 yields $\Omega_{MF}(^2\text{H}) = (\pi/2, \alpha, \pi/2)$. Substitution of these Eulerian angles into Eq. (52) gives

$$A(^1\text{H}) = -\frac{1}{2}S_0^2 - (\sqrt{6}/4)S_2^2, \quad (53a)$$

$$A(^2\text{H}) = \frac{1}{2}(3\cos^2\alpha - 1 + \eta\sin^2\alpha)S_0^2 - (1/2\sqrt{6})[3\sin^2\alpha + \eta(\cos^2\alpha + 1)]S_2^2, \quad (53b)$$

$$A(^{17}\text{O}) = -\frac{1}{2}(1 - \eta)S_0^2 + (1/2\sqrt{6})(3 + \eta)S_2^2, \quad (53c)$$

where we have set $\eta=0$ for ^1H . Some of the terms in these expressions differ in sign from previous results^{23,65}; this is due to different conventions for the molecular coordinate axes (M) and to incorrect orientation of the ^{17}O field gradient principal axes system (F) in previous work. With Eq. (9), the expression (53a) for $A(^1\text{H})$ reduces to S_{yy} , as expected.

As a first approximation we may set $\alpha = 54.74^\circ$ (the tetrahedral angle), $\eta(^2\text{H})=0$, and $\eta(^{17}\text{O})=1$, which results in $-A(^2\text{H}) = A(^{17}\text{O})/2 = S_2^2/\sqrt{6}$. ^2H and ^{17}O data thus give nearly linearly dependent information about $P(\Omega_{DM})$. This unfortunate circumstance has previously been noted by Tricot and Niederberger.^{38,39}

Using η values from Table I, we have, in Fig. 4, plotted the magnitudes of the ratios of residual anisotropies for the three combinations of water nuclei versus the ratio S_2^2/S_0^2 of the two second rank order parameters. The curves are based on the gas phase value $\alpha = 52.22^\circ$, but would be only slightly displaced if one instead were to choose $\alpha = 54.74^\circ$.

As can be seen from Eqs. (25) and (42), NMR data yield information only about the *magnitude* of the residual anisotropy. Consequently, data from two nuclei leaves two possible choices for the value of S_2^2/S_0^2 (cf. Fig. 4) and thus four possible pairs of values for the order parameters. This ambiguity may be partly resolved by studying a third nucleus. Even then, however, the absolute signs of the order parameters remain indeterminate. Assume, for the sake of argument, that the signs can be determined somehow, e.g., with the aid of data from another experimental technique which probes a second rank tensorial interaction. What can we then infer about the orientational probability distribution for the perturbed water molecules? Although it may be possible to rule out a few extreme models, no unique distribution $P(\Omega_{DM})$ can be deduced, because, as has been emphasized above, the order parameters S_0^2 and S_2^2 determine only the $l=2$ terms in the, possibly very slowly converging, expansion (7). This point may be illustrated by a simple example: among the infinitude of distributions $P(\cos\theta_{DM})$ that correspond to $S_0^2=0$ are the following three, physically quite distinct, possibilities

$$P(\cos\theta_{DM}) = \begin{cases} 1, & \cos\theta_{DM} \geq 0 \\ 0, & \cos\theta_{DM} < 0 \end{cases}, \quad \text{or} = \begin{cases} 1, & \cos\theta_{DM} \geq 0 \\ 0, & \cos\theta_{DM} < 0 \end{cases}, \quad (54)$$

or $= \delta(\cos\theta_{DM} - 1/\sqrt{3})$.

In Table II we have collected experimental results for the anisotropy ratios derived from water ^1H , ^2H , and ^{17}O splittings in various anisotropic systems. It is seen that all the $|A(^2\text{H})/A(^1\text{H})|$ ratios are close to 1, whereas the $|A(^{17}\text{O})/A(^2\text{H})|$ ratios are close to 2. From Fig. 4 we see that to each of these ratios corresponds

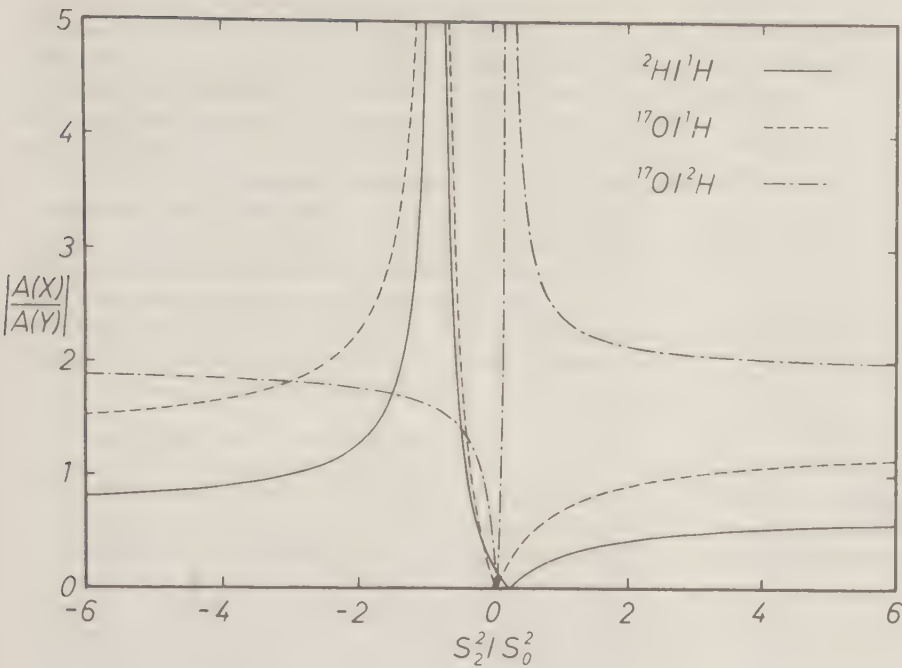


FIG. 4. Ratios of the residual anisotropies for the three combinations of water nuclei vs the ratio of the second rank order parameters. The curves were calculated from Eq. (53) with $\alpha = 52.22^\circ$, $\eta(^2\text{H}) = 0.11$, and $\eta(^{17}\text{O}) = 0.93$.

a possible S_2^2/S_0^2 value close to zero. These alternatives can, however, be discarded, since the curves are nearly vertical in this range, which would, contrary to experimental fact, render the anisotropy ratios extremely sensitive to variations in $P(\Omega_{DM})$. The observed invariance of the ratio $|A(^2\text{H})/A(^1\text{H})|$ has, by several authors,^{23,70,81} been taken as evidence for an orientational distribution function $P(\Omega_{DM})$ which is essentially independent of the molecular details of the surface. Walmsley and Shporer²³ even deduced an invariant S_2^2/S_0^2 value based on the incorrect (see Table II) assumption that also $|A(^{17}\text{O})/A(^2\text{H})| \approx 1$.

In our opinion, these conclusions are unwarranted. The invariance of the anisotropy ratios is simply a con-

sequence of their insensitivity to the value of S_2^2/S_0^2 . Thus the near "degeneracy" for the $^{17}\text{O}/^2\text{H}$ pair makes the $|A(^{17}\text{O})/A(^2\text{H})|$ ratio sensitive to the shape of the orientational distribution only in a very narrow range of S_2^2/S_0^2 values. If values in that range do not occur, which seems to be the case for the systems studied so far, then there is not much information to be gained. The other two anisotropy ratios do carry more information about the orientational distribution. However, when S_0^2 tends to be small, the S_2^2/S_0^2 ratio is largely undetermined. Although the anisotropy ratios are insensitive to the shape of the orientational distribution, this is not so for the individual anisotropies. In fact, the extensive studies of ^2H splittings in amphiphilic mesophases, reported by Persson *et al.*,⁷¹⁻⁷⁶ provide unequivocal evi-

TABLE II. Ratios of residual anisotropies for different water nuclei derived from line splittings in anisotropic systems.

System ^a	$\left \frac{A(^2\text{H})}{A(^1\text{H})} \right $	$\left \frac{A(^{17}\text{O})}{A(^2\text{H})} \right $	Ref.
Collagen, 32–66% RH	1.00		66
Collagen, 36% water (w/w), 25°C	1.02		67
LiDNA, B conformation, 66% RH, ~ 25°C	1.5–1.7		68
LiDNA, C conformation, 66% RH, ~ 25°C	1.2–1.5		68
Na Hectorite, 1–2 cm ³ water/g clay $\Delta(^1\text{H})$ measured at 10°C, $\Delta(^2\text{H})$ at 25°C	1.2		69
Na decyl sulfate: decanol: Na ₂ SO ₄ : D ₂ O, 40:5:5:50% (w/w), nematic phase, 25°C		2.0	38
Na decanoate: decanol: D ₂ O, 30:36:34% (w/w), lamellar phase, 40°C		2.1	38
Na octanoate: decanol: D ₂ O, 8.8:23.8:67.4% (w/w), lamellar phase, 27°C		2.20	13
Na octanoate: D ₂ O, 46.4:53.6% (w/w) hexagonal phase, 27°C		2.12	13
Dipalmitoyl lecithin: D ₂ O, 10 mol D ₂ O/mol DPL, lamellar phase, 20–80°C		2.0–2.5	39

^aRH = relative humidity.

dence for a substantial influence of the molecular nature of the surface (charge density, nature of polar group and counterions, etc.) on the water orientational distribution $P(\Omega_{DM})$.

Walmsley and Shporer²³ argue further that also the relaxation rates for different water nuclei are equal, when normalized to the same interaction strength. They then proceed to explain this experimental "fact" on the basis of the geometry of the interaction tensors. We believe, however, that the finding⁷⁷ that, in one particular system (an aqueous lysozyme solution), the normalized ^1H , ^2H , and ^{17}O longitudinal relaxation rates are of similar magnitude, cannot serve as a basis for the kind of analysis attempted by Walmsley and Shporer.²³ The reason is that the ^1H relaxation rate contains contributions from cross-relaxation^{9,10} and intermolecular dipole-dipole relaxation.⁴⁰ In addition, the ^1H and ^2H rates may contain exchange mediated contributions from nonwater nuclei.^{11,12}

Even if all these complications could be eliminated, there still remains the problem of separating the contributions to the relaxation rates from the fast and slow motions. The predictions of the two-step model for each of these components are as follows. The fast local motion can be described as a rotational diffusion in a slightly anisotropic environment. Within the approximations inherent in the two-step model, the fact that the molecular interaction tensors have different orientations does not affect the fast contribution to the relaxation. For the slow motion, on the other hand, the preceding discussion of the anisotropy ratios applies. Thus, only for the $^2\text{H}/^1\text{H}$ pair is the normalized slow contribution expected to scale (still neglecting the aforementioned complications), whereas the ratio of the normalized slow contributions for ^{17}O and ^2H should be close to 4.

IX. THE RANGE OF THE SURFACE-INDUCED PERTURBATION

It is becoming increasingly clear, that water NMR data are inconsistent with extensive hydration structures that persist over intervals of time which are much longer than the characteristic time for bulk water reorientation.^{13-15,69,70,78-82} The data lend more support to a picture of rapidly ($\sim 10^{-11}$ s) reorienting water molecules with a small residual anisotropy. The approximations inherent in the two-step model, therefore, seem quite reasonable.

Within this model, there are two major problems in the interpretation of relaxation rates: (1) the separation of the amount of perturbed water, as given by the fractions P_i in Eq. (30), from the degree of perturbation, expressed by the spectral density $J(\omega)$; and (2) the separation of the contributions from the fast and slow motions, which will be discussed in the following section. It should be emphasized that the meaning of the term "perturbed water" varies with the experimental technique; in NMR perturbed water is characterized by a residual anisotropy and/or a rate of molecular tumbling significantly different from pure water ($A=0$, and at 300 K, $\tau_r=2.4$ ps).

The observed relaxation rates are, according to Eq. (30), population weighted averages over all water molecules which exchange rapidly compared to their intrinsic relaxation rates. The experimental data indicate that all the perturbed water molecules, with the possible exception of a relatively small number of "buried" or metal-coordinated water molecules,⁸³ is in this rapid exchange domain. The crucial question is then: What is the range of the surface-induced perturbation? Is a two-state model, which recognizes only perturbed and unperturbed water, realistic or do we have to invoke a continuous distribution of correlation times and residual anisotropies?

Whereas simple estimates show that electrostatic interactions, e.g., ion-dipole forces, cannot be significant over more than a few molecular diameters, the surface-induced perturbation of the first water layer could conceivably be propagated over longer distances via successive water-water correlations.⁸⁴ Indeed, such a mechanism, termed hydration force, has been invoked to explain the repulsion between phospholipid bilayers^{85,86} and between mica sheets.^{87,88} This force was found to decrease exponentially with the distance from the surface with a decay length of 0.2 nm for phospholipid and 1.0 nm for mica surfaces. If the residual anisotropy A and the rotational correlation time decay to their bulk values at the same rate as the hydration force, then a two-state model should be reasonable for a decay length of 0.2 nm, corresponding to 95% decay within two molecular diameters, but hardly for a decay length of 1.0 nm.

More direct support for a short-ranged perturbation, and thus for the validity of a two-state model, comes from the observation that the water ^2H splitting in systems containing phospholipid bilayers,² octanoate-decanol bilayers,⁷³ or clay sheets⁸¹ is inversely proportional to water concentration down to water contents corresponding to one or two molecular layers. Recent ^{17}O relaxation studies¹³⁻¹⁵ are also consistent with a similarly short-ranged perturbation. Further evidence against long-range hydration structures comes from permittivity measurements on the lamellar phase (water layer thickness 1-15 nm) of the Aerosol-OT-water system.⁸⁹

The rate of molecular reorientation seems to conform to the same picture; Woessner⁸² recently demonstrated that the longitudinal ^2H relaxation rate varies linearly in the range from 2.7 to 108 water layers between clay sheets. Adopting a two-state model, with one or two perturbed water layers, one finds, for a wide range of systems,^{13-15,82} correlation times for the local water reorientation that are less than an order of magnitude slower than in pure water. Thus, it seems unlikely that more distant water should reorient significantly slower than pure water. Indeed, there may even be water molecules which tumble slightly faster than in pure water. This kind of behavior is predicted from the rotational Smoluchowski equation for a dipole in an external field⁹⁰ and is also, for different reasons, believed to be responsible for the reduction of the water relaxation rates upon addition of "structure-breaking" ions.⁹¹

In conclusion, it appears that the properties of *individual* water molecules, such as the tumbling rate and anisotropy, are significantly affected only to within about two molecular diameters from the surface. However, taken together, the extremely small perturbation of water molecules further removed from the surface may well add up to significant contributions to *collective* properties, such as the force between lamellar surfaces. Consequently, for the purpose of interpreting water NMR data from heterogeneous systems, a two-state model is reasonable, with the understanding that, due to the molecular details of the surface, order parameters and correlation times should be regarded as averages over all rapidly exchanging sites on the surface.

X. SEPARATION OF FAST AND SLOW MOTIONS

There are at least two possible strategies to achieve a separation of the contributions to the relaxation rates from the fast and the slow motional components of the perturbed water molecules. The most obvious approach is to measure the frequency dependence (dispersion) of the relaxation rates, preferably the longitudinal as well as the transverse rate. Since, typically, the correlation times for the fast and slow motions are of the order 10^{-11} and 10^{-8} s, respectively, only the latter will give rise to a frequency dependence at accessible resonance frequencies. What one obtains from such experiments is, apart from the slow correlation time, essentially the two composite quantities $P\tau_f$ and PA^2 , where P is the fraction perturbed water in the two-state model.¹³

The other route to separation of motional components is based on comparisons of isotropic and anisotropic systems with similar local surface structures.¹⁶ In anisotropic systems, the contribution from the slow motion is expected to be reduced or completely absent, whereas the fast motion should be nearly the same for the two kinds of system. The application par excellence of this approach is to aqueous surfactant solutions,¹⁵ where often a transition from an isotropic micellar solution to an anisotropic mesophase occurs within a narrow composition range.⁹² For systems where both of these approaches are feasible, a complete separation of parameters can be accomplished, since the static splittings yield the quantity $P|A|$.

Even when the fast and slow contributions to the relaxation rates have been separated, there remains the problem of identifying the motion(s) responsible for the slow time dependence [cf. Eq. (44)]. Usually, one has to consider chemical exchange, aggregate tumbling, and surface diffusion of, e.g., hydrated ions. The importance of the latter two processes can often be estimated from a knowledge of the relevant diffusion coefficients (from direct measurements or from the aggregate geometry and the Stokes–Einstein or Perrin equations). Information about the water exchange rate can, in certain cases, be obtained from a comparison of isotropic and anisotropic systems [cf. Eq. (51)] or from the proton exchange broadening of the ^{17}O resonance.¹⁴

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APPENDIX A: RELAXATION IN ANISOTROPIC SYSTEMS

In order to derive expressions for the relaxation rates in an anisotropic system, we must evaluate the correlation functions

$$G_k(t) = \langle V_k^{L*}(0) V_k^L(t) \rangle_{LM}. \quad (\text{A1})$$

We shall assume that the relaxation is produced entirely by the fast motion, i.e., by the time dependence in $\Omega_{DM}(t)$. The correlation function (A1) may then be written, in analogy with Eq. (36), as

$$\begin{aligned} G_k(t) = & \sum_m \sum_{m'} \sum_{m''} \sum_q \sum_{q'} \sum_{q''} D_{km}^{2*}(\Omega_{LD}) D_{km}^2(\Omega_{LD}) D_{m'm''}^{2*}(\Omega_{MF}) \\ & \times D_{q'q''}^2(\Omega_{MF}) V_{m'}^F V_{q''}^F \{ \langle D_{mm'}^{2*}[\Omega_{DM}(0)] D_{qq'}^2[\Omega_{DM}(t)] \rangle_{DM} \\ & - \delta_{m0} \delta_{q0} \langle D_{0m'}^{2*}(\Omega_{DM}) \rangle_{DM} \langle D_{0q'}^2(\Omega_{DM}) \rangle_{DM} \}. \end{aligned} \quad (\text{A2})$$

Assume now that there is *fivefold* symmetry around the director, i.e., that $P(\Omega_{DM})$ is invariant to the symmetry operator $D(2\pi/5, 0, 0)$. (In the isotropic case only threefold symmetry was required.) The second rank D elements then transform as components of irreducible representations of the symmetry group of the system and the symmetry theorem (B1) for correlation functions, which is proved in Appendix B, yields

$$\begin{aligned} \langle D_{mm'}^{2*}[\Omega_{DM}(0)] D_{qq'}^2[\Omega_{DM}(t)] \rangle_{DM} \\ = \delta_{mq} \langle D_{mm'}^{2*}[\Omega_{DM}(0)] D_{mq'}^2[\Omega_{DM}(t)] \rangle_{DM}. \end{aligned} \quad (\text{A3})$$

Inserting this result into Eq. (A2) and performing the steps that led from Eq. (37) to (39), we obtain

$$\begin{aligned} G_k(t) = & \sum_m \sum_{m'} \sum_{q'} D_{km}^{2*}(\Omega_{LD}) D_{km}^2(\Omega_{LD}) V_{m'}^F V_{q'}^F \\ & \times [\langle D_{mm'}^{2*}(\Omega_{DF}) D_{mq'}^2(\Omega_{DF}) \rangle_{DF} - \delta_{m0} \langle D_{0m'}^{2*}(\Omega_{DF}) \rangle_{DF} \\ & \times \langle D_{0q'}^2(\Omega_{DF}) \rangle_{DF}] \tilde{G}_f(t), \end{aligned} \quad (\text{A4})$$

where, for simplicity, we have set $\Omega_{MF} = 0$. (The numerical values of the elements $D_{mm'}^{2*}(\Omega_{DF})$ thus depend on the identity of the nucleus considered.) In an isotropic system, $P(\Omega_{LD}) = 1/8\pi^2$, so that the Ω_{LD} dependence in the correlation function disappears by virtue of the orthogonality of the Wigner rotation matrices [cf. Eqs. (36) and (37)]. In an anisotropic system, on the other hand, the correlation functions (A4), and thus also the relaxation rates, depend on the orientation of the director with respect to the external magnetic field.

Consider, for simplicity, an anisotropic system which is aligned with the external magnetic field, thereby making $\theta_{LD} = 0$. Using the product formula for D elements²⁵ as well as the definitions (11) and (17) and evaluating the 3- j symbols, we obtain from Eq. (A4)

$$G_0(t) = (V_0^F)^2 \left\{ \left[\frac{1}{5} + \frac{2}{7} D_{00}^2 + \frac{18}{35} D_{00}^4 - (D_{00}^2)^2 \right] - \frac{2\eta}{\sqrt{6}} \left[\frac{2}{7} (D_{02}^2 + D_{0-2}^2) - \frac{3\sqrt{15}}{35} (D_{02}^4 + D_{0-2}^4) + D_{00}^2 (D_{02}^2 + D_{0-2}^2) \right] + \frac{\eta^2}{6} \left[\frac{2}{5} - \frac{4}{7} D_{00}^2 + \frac{6}{35} D_{00}^4 + \frac{6}{\sqrt{70}} (D_{04}^4 + D_{0-4}^4) - (D_{02}^2 + D_{0-2}^2)^2 \right] \right\} \tilde{G}_f(t), \quad (\text{A5a})$$

$$G_1(t) = (V_0^F)^2 \left\{ \left(\frac{1}{5} + \frac{1}{7} D_{00}^2 - \frac{12}{35} D_{00}^4 \right) - \frac{2\eta}{\sqrt{6}} \left[\frac{1}{7} (D_{02}^2 + D_{0-2}^2) + \frac{2\sqrt{15}}{35} (D_{02}^4 + D_{0-2}^4) \right] + \frac{\eta^2}{6} \left[\frac{2}{5} - \frac{2}{7} D_{00}^2 - \frac{4}{35} D_{00}^4 - \frac{4}{\sqrt{70}} (D_{04}^4 + D_{0-4}^4) \right] \right\} \tilde{G}_f(t), \quad (\text{A5b})$$

$$G_2(t) = (V_0^F)^2 \left\{ \left(\frac{1}{5} - \frac{2}{7} D_{00}^2 + \frac{3}{35} D_{00}^4 \right) - \frac{2\eta}{\sqrt{6}} \left[-\frac{2}{7} (D_{02}^2 + D_{0-2}^2) - \frac{\sqrt{15}}{70} (D_{02}^4 + D_{0-2}^4) \right] + \frac{\eta^2}{6} \left[\frac{2}{5} + \frac{4}{7} D_{00}^2 + \frac{1}{35} D_{00}^4 + \frac{1}{\sqrt{70}} (D_{04}^4 + D_{0-4}^4) \right] \right\} \tilde{G}_f(t), \quad (\text{A5c})$$

where $\langle D_{mm}^i(\Omega_{DF}) \rangle_{DF}$ has been abbreviated by D_{mm}^i . The special case of Eq. (A5) with $\eta=0$ has been given previously by Jacobsen *et al.*,¹⁷ albeit with two erroneous numerical coefficients, and by Freed *et al.*^{93,94}

A simple check of the result (A5) is provided by the requirement that it should behave correctly in the isotropic limit. Summing Eq. (A4), with $\Omega_{LD}=0$, over k , dividing by 5, and using the product formula for D elements and the orthogonality relation for 3- j symbols,²⁵ we obtain the isotropic result (39). Thus

$$\frac{1}{5} \sum_{k=-2}^2 G_k(t, \theta_{LD}=0) = G_f^{\text{isotropic}}(t). \quad (\text{A6})$$

Inserting the $G_k(t)$ from Eq. (A5), we recover the isotropic result (41), as required.

As a rule, the fast motion is rapid compared to the resonance frequency ("extreme narrowing" condition), so that $\tilde{J}_f(0) = \tilde{J}_f(\omega_0) = \tilde{J}_f(2\omega_0)$, where the reduced spectral density $\tilde{J}_f(\omega)$ is the Fourier transform of $\tilde{G}_f(t)$, as in Eq. (28). Even in this case, the correlation functions (A5) lead, in general, to complicated expressions for the relaxation rates. Thus we will give explicit expressions only for a few special cases. The longitudinal relaxation following the application of a nonselective pulse to a collection of spin $I=1$ nuclei, e.g., ^2H , is characterized by a rate⁵⁸

$$R_1 = K[2J_1(\omega_0) + 8J_2(2\omega_0)], \quad (\text{A7})$$

where the constant K is given by Eq. (27c). Inserting the correlation functions (A5), we find that, in the extreme narrowing limit, the fourth rank D elements cancel and

$$R_1 = 2K(V_0^F)^2 \left[1 + \frac{1}{3} \eta^2 - (3 - \frac{1}{3} \eta^2) \langle P_2(\cos\theta_{DF}) \rangle_{DF} + 2A \right] \tilde{J}_f(0), \quad (\text{A8})$$

where P_2 is the second rank Legendre polynomial. If the nondegeneracy of the Zeeman transitions is neglected, the factor 3 multiplying $J_1(\omega_0)$ in Eq. (47) should be replaced by a factor 5 [as in the isotropic case (27b)]. The fourth rank D elements then disappear also from the transverse relaxation rate, which, for $I=1$ and in the extreme narrowing limit, becomes

$$R_2 = 2K(V_0^F)^2 \left[1 + \frac{1}{3} \eta^2 + \frac{1}{2} (3 - \frac{1}{3} \eta^2) \times \langle P_2(\cos\theta_{DF}) \rangle_{DF} - A - \frac{3}{2} A^2 \right] \tilde{J}_f(0). \quad (\text{A9})$$

The special cases of Eqs. (A8) and (A9) with $\eta=0$ agree with the results given by Brown.²² The exact Eq. (47) yields, with $\eta=0$ and in the extreme narrowing limit

$$R_2 = 2K(V_0^F)^2 \left[\frac{4}{5} + \frac{5}{14} \langle P_2(\cos\theta_{DF}) \rangle_{DF} - \frac{3}{2} \langle P_2(\cos\theta_{DF}) \rangle_{DF}^2 + \frac{12}{35} \langle P_4(\cos\theta_{DF}) \rangle_{DF} \right] \tilde{J}_f(0). \quad (\text{A10})$$

APPENDIX B: A SYMMETRY THEOREM FOR TIME CORRELATION FUNCTIONS

Theorem: If the operators S_q^K and $T_{q'}^{K'}$ transform as the components q and q' of the irreducible representations K and K' of the symmetry group of the system, then their time correlation function is nonzero only if they belong to the same component of the same irreducible representation. Furthermore, the value of the correlation function is the same for all components of that irreducible representation, i.e.,

$$\langle S_q^{K*}(0) T_{q'}^{K'}(t) \rangle = \delta_{KK'} \delta_{qq'} \langle S_r^{K*}(0) T_r^{K'}(t) \rangle, \quad (\text{B1})$$

where r denotes any component belonging to K .

Proof: The time correlation function can be written as the trace

$$\langle S_q^{K*}(0) T_{q'}^{K'}(t) \rangle = \text{Tr} \{ S_q^{K*} e^{iHt} T_{q'}^{K'} e^{-iHt} \rho_{\text{eq}} \}. \quad (\text{B2})$$

Since the Hamiltonian H , and thus also the equilibrium density operator ρ_{eq} , is totally symmetric, the operator

$$W_{q'}^{K'}(t) \equiv e^{iHt} T_{q'}^{K'} e^{-iHt} \rho_{\text{eq}} \quad (\text{B3})$$

must be of the same symmetry as $T_{q'}^{K'}$. Expanding the trace in the energy eigenbasis, we find

$$\langle S_q^{K*}(0) T_{q'}^{K'}(t) \rangle = \sum_{\alpha} \sum_M \sum_m \langle \alpha M m | S_q^{K*} W_{q'}^{K'}(t) | \alpha M m \rangle, \quad (\text{B4})$$

where the sums run over all energy eigenvalues α , over all irreducible representations M , and over all degenerate eigenvectors m belonging to each irreducible representation.

To each symmetry operation R in the symmetry group $\{R\}$ of the system there corresponds a unitary operator P_R , which transforms vectors according to

$$P_R |\alpha M m\rangle = \sum_n |\alpha M n\rangle \Gamma_{nm}^M(R) \quad (\text{B5})$$

and operators according to

$$P_R O_q^K P_R^\dagger = \sum_r O_r^K \Gamma_{rq}^K(R), \quad (\text{B6})$$

where the $\Gamma^A(R)$ are the unitary representation matrices.⁹⁵

Using the transformation relations (B5) and (B6), we find for the sum over m in Eq. (B4)

$$\begin{aligned} \sum_m \langle \alpha M m | S_q^{K\dagger} W_q^{K'}(t) | \alpha M m \rangle &= \sum_m \langle \alpha M m | P_R^\dagger P_R S_q^{K\dagger} P_R^\dagger P_R W_q^{K'}(t) P_R^\dagger P_R | \alpha M m \rangle \\ &= \sum_m \sum_n \sum_{n'} \sum_r \sum_{r'} \langle \alpha M n | \Gamma_{nm}^{M*}(R) S_r^{K\dagger} \Gamma_{rq}^{K*}(R) W_{r'}^{K'}(t) \Gamma_{r'q'}^{K'}(R) \Gamma_{n'm}^M(R) | \alpha M n' \rangle \\ &= \sum_r \sum_{r'} \Gamma_{rq}^{K*}(R) \Gamma_{r'q'}^{K'}(R) \sum_n \langle \alpha M n | S_r^{K\dagger} W_{r'}^{K'}(t) | \alpha M n \rangle, \end{aligned} \quad (\text{B7})$$

where the last step follows from the unitarity of the representation matrices.

Since Eq. (B7) is true for any element R of the symmetry group of the system, the equality still holds after summation of both sides of the equation over all the h elements of the group. Using the Great Orthogonality Theorem⁹⁵

$$\sum_R \Gamma_{rq}^{K*}(R) \Gamma_{r'q'}^{K'}(R) = \frac{\hbar}{N_K} \delta_{KK'} \delta_{rr'} \delta_{qq'}, \quad (\text{B8})$$

where N_K is the dimensionality of the K th irreducible representation, we then find

$$\begin{aligned} \sum_m \langle \alpha M m | S_q^{K\dagger} W_q^{K'}(t) | \alpha M m \rangle \\ = \delta_{KK'} \delta_{qq'} \frac{1}{N_K} \sum_n \sum_r \langle \alpha M n | S_r^{K\dagger} W_r^K(t) | \alpha M n \rangle, \end{aligned} \quad (\text{B9})$$

which is independent of q for all α and M . Substitution of this result into Eq. (B4) completes the proof.

The generalization of the theorem to the case where S_q^K and $T_q^{K'}$ transform as components of *reducible* representations is trivial, if the operators are linear. It should also be pointed out that the theorem holds as well for classical correlation functions; the proof for that case can be carried out analogously. Finally, we note that Hubbard's theorem⁹⁶ for time correlation functions of irreducible tensor operators constitutes the special case for spherically symmetric systems of the theorem given here.

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III

Hydration of Ionic Surfactant Micelles from Water Oxygen-17 Magnetic Relaxation

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Water oxygen-17 relaxation rates have been measured for aqueous solutions of micelles composed of ionic surfactants of varying alkyl chain length, head group, and counterion. The concentration of surfactant and salt was also varied. From these measurements, supplemented with relaxation data for short-chain molecules and with quadrupolar splittings from anisotropic mesophases, we derive structural and dynamic information about the molecular details of the water-micelle interaction. Water molecules at the micelle surface reorient anisotropically, typically 2–3 times slower than in pure water. The average lifetime for water molecules associated with sodium dodecyl sulfate micelles is 6–37 ns. The water-hydrocarbon contact in the micellar solutions is equivalent to less than two fully exposed methylene groups per amphiphile. Small head groups and small counterions produce the largest effects on the ^{17}O relaxation rate, as expected from geometrical and electrostatic considerations.

Introduction

There are few systems in which the solute-solvent interaction has more dramatic consequences than in aqueous surfactant solutions. A characteristic feature of these systems is the cooperative self-association of surfactant, i.e., amphiphilic molecules composed of a polar, often charged, part and a relatively large nonpolar part, to form large aggregates, known as micelles. Aggregation typically occurs only above a well-defined surfactant concentration (cmc). Several recent reviews^{1–4} provide extensive accounts of the phenomenon of surfactant association.

The overwhelming majority of experimental and theoretical studies have confirmed the classical picture of

micelles, proposed originally by Hartley.⁵ According to this picture, the micellar aggregate consists of a liquidlike hydrocarbon core, with the charged head groups residing at the surface in contact with the surrounding aqueous medium. Although there has been some controversy^{6–8} about the degree of water penetration into the hydrocarbon core, it seems that no unequivocal evidence of substantial water penetration exists. On the other hand, some water-hydrocarbon contact inevitably exists since most head groups are simply too small to completely cover the curved aggregate surface. Another factor which leads to water-hydrocarbon contact is the so-called “dynamic roughness” of the micelle surface. Thus, Aniansson⁹ es-

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timates an average protrusion of about 1.5 methylene groups in a sodium dodecyl sulfate micelle. A further important characteristic of ionic micellar solutions is the inhomogeneous distribution of counterions, with 40–80 % of the counterions confined to a region extending a few tenths of a nanometer out from the micelle surface.⁴

In theoretical models of micellar solutions, the aqueous phase is usually treated as a continuous dielectric medium. It is clear, however, that a detailed understanding of these systems will require explicit recognition of the molecular nature of the medium. Thus we would like to quantify the strength and range of the water–micelle interaction as well as its dynamic consequences. Quantities related to the amount of interacting water, e.g., “hydration numbers”, have been obtained mainly from transport properties, e.g., intrinsic viscosity,^{10–13} micellar sedimentation and diffusion coefficients,¹¹ and water self-diffusion coefficients,^{14–16} and also from molar volumes.¹⁷ The dynamic behavior, on the other hand, has been probed by various relaxation techniques: magnetic,^{18,19} dielectric^{20,21} or ultrasonic.²²

The main conclusion from the viscosity and diffusion studies of solutions of ionic micelles is that the deduced “hydration numbers” of 4–10 water molecules per surfactant molecule, corresponding to the amount of water moving with the micelle as a kinetic entity, can be fully accounted for by the hydration of the charged head groups and of the associated counterions.²³ This conclusion is in qualitative agreement with the water proton chemical shift and longitudinal relaxation studies of Clifford and Pethica¹⁸ and of Walker,¹⁹ which indicate a reduced water–hydrocarbon contact upon micellization.

As regards the dynamics of the associated water, e.g., reorientational rate and anisotropy and average residence time, considerable uncertainty remains. Due mainly to the influence of hydrocarbon protons on the water proton relaxation behavior, it has not been possible to extract dynamic information from proton relaxation rates.^{18,19} The most detailed studies of the microdynamics of water in micellar solutions are the dielectric relaxation measurements from the Göttingen group.^{20,21} As compared to magnetic relaxation, the dielectric relaxation technique has the advantage of accessibility to frequencies in the gigahertz range. However, the theoretical understanding of dielectric relaxation in terms of molecular parameters is at present rather limited. To interpret dielectric relaxation data one is thus forced to use continuum models involving many adjustable parameters and based on several simplifying assumptions. Nevertheless, the main conclusion from these studies,^{20,21} that the “hydration water” reorients

less than an order of magnitude slower than pure water, is probably indisputable, because of the well-characterized dispersion in the gigahertz range. Finally, mention should be made of a recent ultrasonic relaxation study²² in which a relaxation process below 2 MHz was detected at high surfactant concentrations. The authors suggest that water exchange between the hydration and bulk regions is the underlying process, however, no quantitative analysis was attempted.

In the present contribution we report water ¹⁷O relaxation rates for a variety of ionic surfactant solutions above the cmc, and also for a few nonassociated molecules. After a brief exposé of the relevant relaxation theory, which involves a “two-step model” with explicit reference to the anisotropy in the “bound” water reorientation, we present and interpret the relaxation data in five sections. The first section deals with the extent of water–hydrocarbon contact in micelles and the second with the effect on the ¹⁷O relaxation of alkyl chain length. In the third section we exploit the well-established growth of sodium dodecyl sulfate micelles upon salt addition to estimate the average residence time for water molecules at the micelle surface. Next we consider the analogous case of the sphere-to-rod transition for hexadecyltrimethylammonium bromide micelles and, finally, we discuss the effect of head group and counterion on the hydration.

Experimental Section

Chemicals. The surfactants were obtained from the following sources: acetic acid (Merck, Suprapur), propanoic acid (BDH, min 99%), octanoic, dodecanoic, tetradecanoic, and hexadecanoic acids (BDH, specially pure), sodium dodecyl sulfate (BDH, specially purified for biochemical work), hexadecyltrimethylammonium bromide (BDH and Merck).

The potassium salts were prepared by neutralization with KOH, and then freeze dried and recrystallized from absolute ethanol. The molar masses were checked by titration with perchloric acid in glacial acetic acid. The sodium and cesium salts were prepared by neutralization with NaOH (EKA) or CsOH (Ventron). Added NaCl was from Merck (Suprapur).

Hexadecyltrimethylammonium chloride was prepared by transferring the bromide salt to the hydroxide form on a Dowex 21 K ion exchanger (BDH). The hydroxide was immediately neutralized with HCl to pH 4–5, whereafter the solution was lyophilized and the chloride salt recrystallized from acetone.

Aqueous surfactant solutions were made from doubly distilled (quartz apparatus) water, enriched to about 1 % in ¹⁷O by addition of 10 atom % H₂¹⁷O (Biogenzia Leman). The solution pH was adjusted, with KOH, NaOH, or HCl, sufficiently far from neutral (cf. Table I) for the proton exchange broadening^{30,61} to be negligible.

Relaxation Measurements. Oxygen-17 magnetic relaxation rates were measured at 13.56 MHz on a modified Varian XL-100-15 Fourier transform spectrometer and at 34.56 MHz on a home-built Fourier transform spectrometer with a 6-T wide-bore magnet from Oxford Instrument Co.

Longitudinal relaxation rates were measured by inversion recovery (π – τ – $\pi/2$ pulse sequences). Each R_1 value is the result of a least-squares fit to the magnetization vs. delay time for eight different τ values. Transverse relaxation rates were obtained from the line width ($\Delta\nu_{1/2}$) at half-amplitude of the absorption curve according to $R_2 = \pi\Delta\nu_{1/2}$. The contribution to the line width from magnetic field inhomogeneity was eliminated by measuring at 3–6 concentrations and taking the slope $\partial R_2/\partial m$, or by sub-

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tracting the relaxation rate for a sample of pure water (pH 2.7) measured at the same temperature.

Two to four independent measurements of R_1 as well as of R_2 were performed on each sample. In those cases where no significant difference between R_1 and R_2 (or the corresponding slopes) was observed, the reported values are averages over all R_1 and R_2 data. The quantity $n(R_B - R_F)$, reported in Table I, was obtained according to eq 2 as explained in a footnote to the table. The experiments were carried out at a probe temperature of 27.4 °C, which was kept constant to within ± 0.2 °C by the passage of dry thermostated air.

Results and Discussion

General Considerations. In aqueous surfactant solutions the ^{17}O nuclei are distributed over several motional states with different intrinsic relaxation rates but with negligible chemical shift differences. If the exchange of water molecules between these states is fast compared to the intrinsic relaxation rates (see below), then the total relaxation rate may be decomposed^{24,25} according to eq 1, where the sum runs over all states and P_i is the fractional population in state i .

$$R = \sum_i P_i R_i \quad (1)$$

For aqueous surfactant solutions above the cmc, it is reasonable to consider three states: water "bound" to micelles, water "bound" to monomeric (nonmicellized) amphiphiles, and "free" water. Furthermore, we will adopt the phase separation model,¹⁻⁴ according to which the monomer concentration remains constant above the cmc. For a fast exchange three-state model, the excess relaxation rate is thus given by eq 2. In eq 2, m is the total am-

$$R_{\text{ex}} = R - R_F = \frac{n_{\text{mon}} m}{55.5} (R_{\text{mon}} - R_F) \quad m < m_{\text{cmc}} \quad (2a)$$

$$R_{\text{ex}} = R - R_F = \frac{n_{\text{mon}} m_{\text{cmc}}}{55.5} (R_{\text{mon}} - R_F) + \frac{n_{\text{mic}} (m - m_{\text{cmc}})}{55.5} (R_{\text{mic}} - R_F) \quad m > m_{\text{cmc}} \quad (2b)$$

phiphile molality, n is the number of motionally perturbed water molecules per amphiphile, and the subscripts F, mon, and mic refer to "free" water and water "bound" to monomeric or micellized amphiphiles, respectively. For the variation of the excess relaxation rate with the total amphiphile molality we find

$$\partial R_{\text{ex}} / \partial m = \frac{n}{55.5} (R_B - R_F) \quad (3)$$

where n and R_B refer to monomeric or micellized amphiphiles depending on whether m is lower or higher than m_{cmc} .

It is well-known¹⁻⁴ that the phase separation model is not strictly valid, in particular, the monomer concentration decreases above the cmc.^{16,62} For the present purposes, however, eq 2 and 3 are excellent approximations. This is so because, with one exception, our data refer to concentrations that are so much larger than the cmc (Table I) that any variation in the small contribution to the ^{17}O relaxation rate from monomeric amphiphiles must necessarily be small. The exception is octanoate, which has a relatively high cmc. The data of Puyal¹⁶ for sodium octanoate show, however, that the effect of decreasing

monomer concentration is merely 2%, which is less than the standard deviation in $\partial R_{\text{ex}} / \partial m$.

Equation 3 contains two unknowns: n and R_B . (R_F is taken to be equal to the relaxation rate for pure water, which was determined to be $129.7 \pm 2 \text{ s}^{-1}$ at 27.4 °C.) The quantity n is a measure of the number of water molecules, per amphiphile molecule, whose reorientational motion is significantly perturbed. The interpretation of the intrinsic relaxation rate R_B for these n water molecules depends on the model chosen to describe the molecular motions. The simplest model considers the "bound" water molecules to reorient isotropically with a rotational correlation time τ_{CB} , in which case R_B is given²⁶ by eq 4. The water ^{17}O

$$R_B = \frac{12\pi^2}{125} \chi^2 (1 + \eta^2/3) \tau_{\text{CB}} \quad (4)$$

quadrupole coupling constant $\chi = 6.67 \text{ MHz}$,^{27,28} and is virtually independent of the molecular environment. The asymmetry parameter for the electric field gradient is taken to be the same as in ice:²⁹ $\eta = 0.93$.

As will be clear from the following, the isotropic reorientation model, underlying eq 4, cannot satisfactorily explain all our data. This model has also been found inadequate in connection with recent ^{17}O studies^{28,30} of aqueous solutions of macromolecules. In a more realistic model one has to recognize that the water-micelle interaction inevitably induces some anisotropy in the reorientation of the interacting water molecules. This local anisotropic reorientation can only partially average the quadrupolar interaction,^{27,31} the remaining part being averaged out by a slower motion, e.g., exchange of water molecules with the bulk or reorientation of the entire micelle. We will now assume that (1) the fast and slow motions occur independently and on different time scales, (2) there is local threefold symmetry around the normal to the micelle surface, and (3) the anisotropy is small. It can then be shown^{27,31} that R_B can be decomposed into one contribution from the fast (f) motion and another contribution from the slow (s) motion, as in eq 5.

$$R_B = \frac{12\pi^2}{125} \chi^2 [(1 + \eta^2/3 - A^2) \tau_{\text{CB}}^f + A^2 \tau_{\text{CB}}^s] \quad (5)$$

The residual anisotropy A , the magnitude of which is confined to the range $[0,1]$, is determined by the asymmetry parameter η and by the orientational probability distribution for the "bound" water molecules with respect to the normal to the micelle surface.²⁷ For completely isotropic reorientation, $A = 0$ and eq 5 reduces to eq 4. From eq 5, which is valid only for $A^2 \ll 1$, it is seen that for the slow motion to contribute significantly to the relaxation rate, it must be slower than the fast motion by a factor of the order of $1/A^2$. If both micelle reorientation (correlation time τ_{rB}) and water exchange (average lifetime τ_{IB}) contribute to the slow motion, then this may be characterized by an effective correlation time²⁵ according to eq 6.

$$\frac{1}{\tau_{\text{CB}}^s} = \frac{1}{\tau_{\text{rB}}} + \frac{1}{\tau_{\text{IB}}} \quad (6)$$

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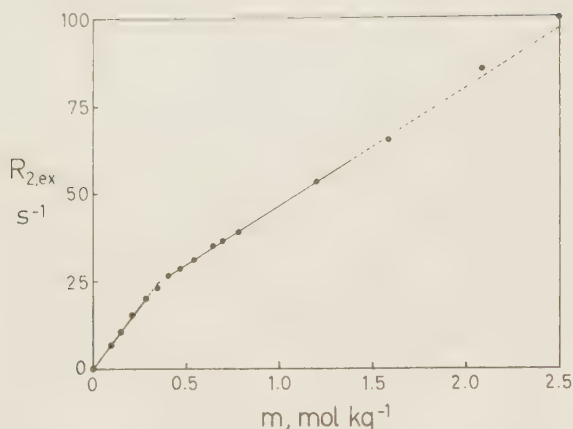


Figure 1. Water ^{17}O transverse excess relaxation rate vs. molality of potassium octanoate at 27.7 °C and 13.56 MHz. The lines were obtained by least-squares fits to the data points connected by solid lines.

If the slow motion is not fast compared to the inverse angular resonance frequency $1/\omega_0$, then the longitudinal and transverse relaxation rates become unequal. In eq 4 and 5, τ_{CB} and τ_{CB}^s , respectively, should then be multiplied by^{32,33}

$$\frac{0.2}{1 + (\omega_0\tau_{\text{CB}})^2} + \frac{0.8}{1 + (2\omega_0\tau_{\text{CB}}^s)^2} \quad (7a)$$

for the longitudinal relaxation rate, and by

$$0.3 + \frac{0.5}{1 + (\omega_0\tau_{\text{CB}})^2} + \frac{0.2}{1 + (2\omega_0\tau_{\text{CB}}^s)^2} \quad (7b)$$

for the transverse relaxation rate.

Extent of Water-Hydrocarbon Contact. The variation of the water ^{17}O excess relaxation rate ($R_1 = R_2$) with concentration of potassium octanoate is shown in Figure 1. There are two linear regions interrupted by a well-defined change of slope at 0.350 mol kg⁻¹, which we identify as the cmc. (Literature cmc values³⁴⁻³⁹ fall in the range 0.35–0.45 mol kg⁻¹.) The reduction in the quantity $n(R_B - R_F)$, obtained from the slopes according to eq 3, from 3.90×10^3 below the cmc to 1.86×10^3 above the cmc (Table I), indicates a substantial reduction of the water-hydrocarbon contact upon micellization. (As noted above, the effect of decreasing monomer concentration above the cmc is negligible.)

In order to quantify this conclusion, we performed measurements on solutions of two short-chain potassium alkanoates. From the data in Table I it is seen that octanoate micelles produce virtually the same effect on the water ^{17}O relaxation as does propionate. We can thus infer that the water-hydrocarbon contact in potassium octanoate micelles corresponds to at most two fully exposed methylene groups per amphiphile. This must be taken as an upper limit since, as discussed above (eq 5), there may be a contribution from slow motions to the relaxation rate for the micellar solution. On the other hand, a much smaller hydrocarbon exposure is unlikely on purely geometrical grounds. Thus, in a molecular model with an aggregation number⁴⁰ of 11 only about half of the "surface

TABLE I: Water ^{17}O Relaxation Data for Aqueous Surfactant Solutions at 27.4 ± 0.2 °C

surfactant ^a	cmc, ^b mol kg ⁻¹	m, mol kg ⁻¹	pH	$10^{-3} n \cdot$ $(R_B - R_F),^c$ s ⁻¹
CH ₃ CO ₂ K		0.49	12.0	1.38 ± 0.05
CH ₃ CH ₂ CO ₂ K		0.56	12.2	1.84 ± 0.05
C ₇ CO ₂ K	0.35	0.10–0.32	12.1	3.90 ± 0.14
C ₇ CO ₂ K	0.35	0.45–1.00	12.1	1.86 ± 0.04
C ₁₁ CO ₂ Na	0.023	0.42	11.8	2.93 ± 0.20
C ₁₁ CO ₂ K	0.024	0.44	10.5	1.99 ± 0.20
C ₁₁ CO ₂ Cs	0.025	0.45	12.3	2.18 ± 0.20
C ₁₃ CO ₂ K	0.006	0.10–0.50	12.0	2.19 ± 0.09
C ₁₅ CO ₂ K	0.002	0.10–0.55	12.0	2.09 ± 0.06
				(R ₁)
				2.48 ± 0.18
				(R ₂)
C ₁₂ OSO ₃ Na	0.008	0.10–0.90	10.9	1.77 ± 0.05
C ₁₂ OSO ₃ Na	0.001	0.10 + 0.38 m NaCl	10.9	3.88 ± 0.30
C ₁₂ OSO ₃ Na	<0.001	0.10 + 0.72 m NaCl	10.9	4.42 ± 0.50
(CH ₃) ₄ NBr		1.0–3.7	1–2	1.18^d
(C ₄ H ₉) ₄ NBr		0.6–2.4	1–2	8.06^d
C ₁₆ N(CH ₃) ₃ Cl	0.001	0.18	3.6	2.99 ± 0.30
C ₁₆ N(CH ₃) ₃ Br	0.001	0.18	3.4	1.88 ± 0.30
C ₁₆ N(CH ₃) ₃ Br	0.001	0.57	3.4	2.19 ± 0.10

^a C_n denotes the normal alkyl chain CH₃(CH₂)_{n-1}.

^b From ref 34, except for C₇CO₂K, the cmc of which is taken from Figure 1. ^c With one exception, we found no significant difference between R₁ and R₂ and no significant frequency dependence between 13.56 and 34.56 MHz. The exception is C₁₅CO₂K, for which R₁ ≠ R₂ at 34.56 MHz. The quantity $n(R_B - R_F)$ was obtained, according to eq 2, from least-squares fits to 5–12 data points (each derived from 2–4 measurements) in the indicated concentration range (± 1 standard deviation), or from measurements at a single concentration ($\pm$ estimated uncertainty). The data for the dodecanoates have been corrected for the monomer contribution (5–10 %), using $n(R_{\text{mon}} - R_F) = 5.5 \times 10^3$ (extrapolated from the monomer data). ^d From ref 41.

area" is occupied by carboxylate groups.

The conclusion that the water-hydrocarbon contact corresponds to less than two fully exposed methylene groups holds also for micelles composed of the longer-chain alkanoates. A longer chain results in a slightly enhanced relaxation rate (Table I), which, however, is due to an increasing contribution from slow motions. This point is discussed in the following section.

The water-hydrocarbon contact in hexadecyltrimethylammonium bromide micelles may be estimated with the aid of ^{17}O relaxation rates for short-chain tetraalkylammonium bromides reported by Fister and Hertz⁴¹ (included in Table I). A comparison with the micelle data shows that an upper limit of two fully exposed methylene groups is reasonable also for hexadecyltrimethylammonium bromide micelles.

Effect of Alkyl Chain Length. The effect of alkyl chain length, i.e., of micelle size, on the water ^{17}O relaxation rate was investigated for potassium alkanoates with 8, 12, 14, and 16 carbon atoms. The data in Table I reveal a monotonic increase in relaxation rate with increasing chain length. From geometrical considerations, it is clear that the area per head group (at a surface which passes through the head groups) must decrease as the micelle grows ra-

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dially.⁴² (This effect, which is quite small, is a consequence of the assumption of a constant area per surfactant molecule at the surface of the hydrocarbon core.) One would thus expect the relaxation rate to decrease somewhat with increasing chain length, contrary to our observations. We therefore conclude that the effect of decreasing water-hydrocarbon contact is overcompensated by a contribution from slow motions according to eq 5. If micelle reorientation contributes to $\tau_{\text{CB}}^{\text{a}}$ (cf. eq 6), this slow contribution should increase with the chain length. This follows from the fact that a longer alkyl chain leads to a larger micelle per se and also increases the aggregation number. (According to the Debye-Stokes-Einstein relation, the rotational correlation time τ_{RB} , appearing in eq 6, is proportional to the cube of the micelle radius.)

For hexadecanoate micelles we observed a significant difference between the longitudinal and transverse relaxation rates at a resonance frequency of 34.56 MHz (Table I). This enables us to estimate the slow correlation time $\tau_{\text{CB}}^{\text{a}}$, if we assume that the fast contribution to the relaxation rates is the same as for acetate. (As noted above, the water-hydrocarbon contact should be smaller for hexadecanoate micelles than for octanoate micelles.) Inserting data from Table I into eq 3, 5, and 7 we thus find $\tau_{\text{CB}}^{\text{a}} = 3$ ns. This figure agrees well with the observed maximum in the longitudinal relaxation rate vs. chain length (Table I), although this maximum is barely significant by itself. From eq 7a one can thus infer that R_1 should exhibit a maximum at $\omega_0\tau_{\text{CB}}^{\text{a}} = 0.6158$, which, at a resonance frequency of 34.56 MHz, corresponds to $\tau_{\text{CB}}^{\text{a}} = 2.8$ ns.

With this estimate for $\tau_{\text{CB}}^{\text{a}}$, it can be shown that the isotropic motion model, i.e., eq 4, is physically unreasonable. Thus $n(R_{\text{B}} - R_{\text{F}}) = 2.09 \times 10^3 \text{ s}^{-1}$ and $\tau_{\text{CB}}^{\text{a}} = 3$ ns for hexadecanoate micelles yield, with eq 4 and 7a, the completely absurd result: $n = 0.03$. This clearly demonstrates that it is necessary to take into account explicitly the consequences of the anisotropy in the "bound" water reorientation, as we have done in eq 5.

NaDS Micelles at High NaCl Concentration. From several light-scattering studies,⁴³⁻⁴⁶ it has been inferred that sodium dodecyl sulfate (NaDS) micelles, at high NaCl concentrations, grow laterally to form large rod-shaped aggregates exceeding 50 nm in length. If the slow correlation time $\tau_{\text{CB}}^{\text{a}}$, entering in eq 5, were determined solely by aggregate reorientation, then one would expect that NaCl addition to NaDS micelle solutions should increase the transverse ^{17}O relaxation rate by orders of magnitude or even lead to quadrupolar splittings. As can be seen from Table I, this is not the case; the relaxation rate is enhanced by merely a factor of 2.5. This observation implies that $\tau_{\text{CB}}^{\text{a}}$ is controlled, to a large extent, by a more rapid motion, which we identify as exchange of water molecules between the "free" and "bound" states. On the basis of this interpretation, we will now proceed to estimate the average residence time τ_{IB} for water molecules associated with the micelle surface.

From the dimensions⁴³⁻⁴⁶ of the rod-shaped NaDS micelles and with the aid of Perrin's equations⁴⁷ we find an effective⁴⁸ rotational correlation time $\tau_{\text{RB}} \approx 2 \mu\text{s}$. Antici-

pating the result of the calculation, we assume that this is so much larger than the lifetime τ_{IB} that, according to eq 6, $\tau_{\text{CB}}^{\text{a}} = \tau_{\text{IB}}$. To proceed, we need an estimate of the residual anisotropy A , appearing in eq 5.

The local environment for water molecules interacting with the sulfate head groups is undoubtedly very nearly the same in the rod-shaped aggregates under discussion and in the hexagonal mesophase consisting of ordered rod-shaped aggregates. Since this latter system is anisotropic one obtains quadrupolar splittings in the water deuteron or ^{17}O spectra, from which the residual anisotropy can be extracted. Since the water ^{17}O residual anisotropy is simply twice that for water deuterons,^{27,49} we have not measured the ^{17}O splitting but have used literature data⁵⁰ for the deuteron splitting in the hexagonal phase of the D_2O -NaDS system. The observed splitting is 560 Hz for 21.6 mol of D_2O per mol of NaDS. Using the equation^{27,31} for the quadrupolar splitting in a powder sample and a deuteron quadrupole coupling constant²⁷ of 220 kHz, we find $|A| = 0.29/n$, where n is the water "coordination number". We have then multiplied by a factor of 2 to obtain the local anisotropy^{27,31} and by another factor of 2 to convert to the ^{17}O residual anisotropy, as noted above.

We can now substitute $\chi = 6.67 \text{ MHz}$, $\eta = 0.93$, and $|A| = 0.29/n$ into eq 5 for R_{B} , which on combination with the value $n(R_{\text{B}} - R_{\text{F}}) = (4.42 \pm 0.50) \times 10^3$, corresponding to the highest NaCl concentration in Table I, and the known value $R_{\text{F}} = 129.7 \text{ s}^{-1}$, yields an expression for the lifetime τ_{IB} as a function of n and $\tau_{\text{CB}}^{\text{f}}$. It seems reasonable to use a "coordination number" n in the range 6-9, in accordance with viscosity data.^{10,51} The fast correlation time $\tau_{\text{CB}}^{\text{f}}$ is certainly not shorter than 2.38 ps, which is the value for pure water at 27.4 °C. An upper limit is furnished by the relaxation rate for salt-free NaDS micelles (Table I), if we neglect the contribution from the slow motions in this case. It is found that values of n in the range 6-9 correspond to $\tau_{\text{CB}}^{\text{f}}$ values of 3.0 ± 0.5 times the pure water value. Finally, we go back to the expression for τ_{IB} , to find that values of n in the range 6-9 together with $\tau_{\text{CB}}^{\text{f}}$ values 1-3 times longer than for pure water correspond to lifetimes in the relatively narrow range 6-11 ns. Since this actually refers to an effective correlation time, in the sense of eq 7, the upper limit should be multiplied by 1/0.3. The final result is $6 < \tau_{\text{IB}} < 37$ ns.

The Sphere-to-Rod Transition for HTABr Micelles. In the absence of added salt, hexadecyltrimethylammonium bromide (HTABr) micelles undergo a change, at about 0.3 mol kg^{-1} , from an essentially spherical to a cylindrical shape. Upon further increase in concentration, the rodlike aggregates grow along the cylindrical axis. This transition gives rise to dramatic changes in physical properties such as reduced viscosity,¹² light scattering,¹² small angle X-ray scattering,⁵² transverse magnetic relaxation rates of ^{14}N (head groups)⁵³ and of ^{81}Br (counterions),⁵⁴ and anisotropy of the electrical conductivity in oriented solutions.⁵⁵ The increase in the water ^{17}O relaxation rate (Table I), however, is quite small, in fact barely significant. The explanation is most probably the same as in the case of NaDS, i.e., the residual anisotropy is averaged out, not by aggregate re-

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orientation, but by water exchange. (The effective rotational correlation time, as deduced in the ^{14}N relaxation study,⁵³ exceeds 340 ns.)

The approach used in the preceding section to estimate the water lifetime for NaDS micelles cannot, however, be used for HTABr micelles. The reason is that no independent information about the residual anisotropy is available. Thus no resolved deuteron splittings could be observed in a study⁵⁶ of the hexagonal phase of the D_2O -HTABr system, indicating a very small anisotropy. This is not surprising, considering that the methyl groups act to keep the water molecules at some distance from the charge. The small residual anisotropy for water associated with the trimethylammonium group is also consistent with the insignificant effect of the sphere-to-rod transition on the ^{17}O relaxation rate, as compared to the transition in NaDS.

It should be pointed out here that the extremely large "hydration numbers" ($n = 60\text{--}70$) suggested for HTABr micelles by Ekwall et al.¹² receive no support from our data. They are probably an artifact arising from the electroviscous effect. In fact, the water-HTABr interaction appears to be very weak. Thus Mukerjee¹⁰ has estimated, from viscosity data, a hydration number of 4.1 ± 1.3 for tetradecyltrimethylammonium chloride micelles. And, as the data in Table I show, HTABr micelles produce a considerably smaller ^{17}O relaxation enhancement than do HTACl micelles.

Effect of Counterion and Head Group. The effect of the nature of the counterion on the water ^{17}O relaxation rate was investigated for dodecanoate micelles and for hexadecyltrimethylammonium micelles. In the former case we found (Table I) that sodium counterions are substantially more effective than either potassium or cesium ions in enhancing the ^{17}O relaxation rate. It is known⁶⁷ that all three counterions retain their primary hydration upon association to alkanoate micelles. Consequently, the origin of the difference must be that the smaller size of the sodium ions results in a stronger dynamical perturbation of the adjacent water molecules. (This effect on the ^{17}O relaxation is likely to dominate over the effects caused by the higher aggregation number and the more extensive counterion association for CsDS as compared to NaDS, recently reported⁶² by Frahm et al. Indeed, if these were the only counterion effects the ^{17}O relaxation rate would, contrary to observation, be largest for CsDS.) The difference in the ^{17}O relaxation enhancement between sodium and potassium dodecanoate micelles is about three times larger than the difference between NaCl and KCl in the absence of surfactant (unpublished data). The micelles thus have the effect of enhancing the difference in "hydration" between Na^+ and K^+ . This may be due to the fact that the proximity of a large hydrocarbon core with low relative permittivity acts to enhance all electrostatic interactions in the adjacent aqueous region.⁶⁸

It has not been conclusively demonstrated whether chloride and bromide ions retain their primary hydration upon association to alkyl trimethylammonium micelles.^{3,4} However, in view of the striking differences between HTACl and HTABr as regards micelle shape at high concentration,⁵⁹ it is plausible that associated Cl^- and Br^-

differ in hydration. The much larger effect of HTACl micelles, as compared to HTABr micelles (Table I), is thus probably due partly to the different ionic radii and partly to exclusion of some hydration water upon Br^- association.

To get an idea of the importance of the nature of the head group in determining the water ^{17}O relaxation rate, we may compare the data in Table I for NaDS (salt-free) and sodium dodecanoate micelles. It is seen that the carboxylate group produces a much larger effect than the sulfate group. This difference can be accounted for qualitatively on the basis of the smaller size of the COO^- group, relative to the OSO_3^- group. Consequently, there is more space available for water molecules to penetrate between the head groups in the alkanoate micelles.

Conclusions and Summary

The present study confirms our previous^{28,30} conclusion that water ^{17}O relaxation in aqueous solutions of macromolecules or large molecular aggregates cannot be satisfactorily explained by a simple two-state model in which each state is characterized by a single correlation time. Rather, one must introduce two correlation times to describe the stepwise averaging of the quadrupolar interaction in the "bound" state. The contributions from the fast and slow motions to the relaxation rate are often of comparable magnitude when the slow correlation time is in the nanosecond range. Micellar systems are ideally suited for application of the two-step model, because of their simple structure and because the weighting factor for the slow component, i.e., the square of the residual anisotropy, often can be obtained from quadrupolar splittings in the corresponding anisotropic mesophases.

The rate of local water reorientation at the micelle surface is typically 2–3 times slower than in pure water. This is also true for the hydration water of small solutes and agrees with results from dielectric relaxation studies.^{20,21,60} The residual anisotropy is averaged out mainly by micelle reorientation for small micelles and mainly by water exchange for large micelles. The average lifetime for water molecules associated with sodium dodecyl sulfate micelles is between 6 and 37 ns.

No long-range water-micelle interaction is indicated by our data. For potassium octanoate micelles, the ^{17}O relaxation enhancement corresponds to hydration of the carboxylate head groups, the potassium counterions, and a water-hydrocarbon contact equivalent to less than two fully exposed methylene groups. For longer-chain micelles the water-hydrocarbon contact is of similar magnitude. Small head groups permit more water to penetrate between themselves, as evidenced by the larger effect on the ^{17}O relaxation rate of micelles with carboxylate head groups as compared to those with sulfate head groups. The influence of counterions on the ^{17}O relaxation rate can be explained in terms of the ionic radii and a possible dehydration accompanying Br^- association to hexadecyltrimethylammonium micelles.

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IV

Water Oxygen-17 Magnetic Relaxation in Polyelectrolyte Solutions

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Water oxygen-17 longitudinal and transverse relaxation rates have been measured at two frequencies for aqueous solutions of poly(acrylic acid) and poly(methacrylic acid) under conditions of variable temperature, concentration and degree of dissociation. The proton-exchange broadening of the ^{17}O resonance from these polyacid solutions has also been investigated. The data show that the residence time for water molecules interacting with the polyacid is of the order of 10^{-8} s, during which time they reorient anisotropically, an order of magnitude slower than bulk water, and engage in rapid proton transfer with acidic groups. The motional perturbation of associated water is to a large extent electrostatically induced. A new method for determining an upper limit for the lifetime of 'bound' water from the proton-exchange broadening is employed and the necessary equations are derived.

The perturbing effect of macromolecules in aqueous solution on the structure and dynamics of water, commonly referred to by the imprecise term 'hydration', has been intensely studied in recent years.¹ Before the ultimate goal of a full understanding of the interaction of water with complex biological structures can be accomplished, it will be necessary to study a wide variety of simpler model systems. One class of systems, which shares important features with many biological macromolecules, is aqueous solutions of synthetic linear polyelectrolytes. Of the various manifestations of the water-macromolecule interaction, effects on the rate and anisotropy of water reorientation, as well as the average residence time of a water molecule in the perturbed region, are probably most directly studied through the magnetic relaxation of solvent nuclei.

In the present investigation of aqueous solutions of poly(acrylic acid) (PAA) and poly(methacrylic acid) (PMA) we have studied the magnetic relaxation of water oxygen-17 nuclei. This nucleus is preferable to the other two accessible solvent nuclei, the proton and the deuteron, for several reasons. The ^{17}O nucleus relaxes through the interaction of its electric quadrupole moment with the field gradient generated by the charge distribution of the water molecule. The virtual absence of intermolecular contributions greatly simplifies the molecular interpretation of experimental relaxation rates.¹⁶ The large magnitude of the quadrupolar interaction leads to observable relaxation enhancements at comparatively low polyelectrolyte concentrations and makes the ^{17}O relaxation rates much less sensitive to paramagnetic impurities, particularly in comparison with proton relaxation. Furthermore, it has been shown that, in aqueous solutions of PAA and PMA, the deuteron relaxation is determined by the rapidly exchanging acidic deuterons on the polyacids and thus cannot yield information on the state of water in these systems.^{3,4}

EXPERIMENTAL

CHEMICALS

Aqueous solutions of poly(acrylic acid) (25%) and poly(methacrylic acid) (20%) were obtained from B.D.H. Chemicals. The degree of polymerization for the PAA preparation is *ca.* 3200 according to the manufacturer. Since no such information was available for the PMA preparation, we determined the intrinsic viscosity at 30.0 °C and pH 2.7. The value thus obtained, $[\eta] = 5.8 \text{ cm}^3 \text{ g}^{-1}$, corresponds⁵ to a degree of polymerization of *ca.* 90. Polyacid solutions were made by dilution with doubly distilled water (quartz apparatus) and titrated to complete dissociation ($\alpha = 1$) with NaOH prior to relaxation measurements. The sodium-ion concentration was thus, at all degrees of dissociation, equal to or in slight excess of the monomer concentration. Polyacid concentrations are given as mol monomer per kg H_2O (*m*), throughout this paper. Samples of *ca.* 4 g polyacid solution, enriched to *ca.* 1% in ^{17}O , were prepared in n.m.r. tubes with 12 mm outer diameter. H_2O enriched to 10 atom % in ^{17}O was obtained from Biogenzia Lemania, Lausanne. Propionic acid and isobutyric acid were from B.D.H. Chemicals and Th. Schuchardt GmbH, respectively.

TITRATIONS AND pH MEASUREMENTS

pH was varied by adding small volumes of concentrated HCl solutions to the n.m.r. samples. Relaxation rates from the titration experiments (fig. 3) were corrected for dilution assuming proportionality between excess rates and monomer molality. This correction, which is largest at $\alpha = 0$, never exceeds 8%.

pH was measured in the n.m.r. tubes at room temperature with Radiometer PHM 52 or PHM 64 pH meters, equipped with Radiometer GK2322C combination electrodes. Corrections for the sodium error were made according to a nomogram supplied by the manufacturer.

The degree of dissociation, α , of the polyacids as a function of pH was determined through a separate potentiometric titration at each polyacid concentration. From the pH of the solution $[\text{H}_3\text{O}^+]$ or $[\text{OH}^-]$ was calculated using operational activity coefficients (determined in the absence of polyacid). The fraction charged monomers then follows from stoichiometric considerations.

RELAXATION MEASUREMENTS

Oxygen-17 magnetic relaxation rates were measured at 13.56 MHz on a modified Varian XL-100-15 Fourier-transform spectrometer and at 34.56 MHz on a home-built Fourier-transform spectrometer equipped with 6 T wide-bore magnet from the Oxford Instrument Co.

Longitudinal relaxation rates (R_1) were measured with the inversion recovery method (π - τ - $\pi/2$ pulse sequences). Each R_1 value is the result of a least-squares fit of the magnetization plotted against delay time for ten different τ values. Transverse relaxation rates (R_2) were obtained from the linewidth ($\Delta\nu_{\text{obs}}$) at half amplitude of the absorption spectra according to $R_{2,\text{obs}} = \pi\Delta\nu_{\text{obs}}$. Reported R_2 values are averages of 2-4 spectra. The precision was better than $\pm 2 \text{ s}^{-1}$. The excess relaxation rates, defined by eqn (8), were calculated as

$$R_{i,\text{ex}} = R_{i,\text{obs}} - R_{i,\text{ref}} \quad (i = 1, 2).$$

$R_{i,\text{obs}}$ is the relaxation rate (or half-width times π) observed for a polyacid solution and $R_{i,\text{ref}}$ is the same quantity for a sealed sample of H_2O at pH 2.7, measured at the same temperature. Although $R_1 = R_2$ for pure water, $R_{2,\text{ref}} > R_{1,\text{ref}}$ due to a contribution (*ca.* 3 s^{-1}) to the linewidth from magnetic-field inhomogeneity. In the calculation of $R_{i,\text{ex}}$ this contribution cancels. From a large number of measurements we have found the true ^{17}O relaxation rate in pure water [R_F in eqn (8)] at 28.0 °C to be $127.3 \pm 2 \text{ s}^{-1}$.

The experiments were carried out at probe temperatures ranging from 27.4 to 28.5 °C and the data were subsequently normalized, using the temperature-dependence data in fig. 1, to 28.0 °C, unless otherwise stated. These corrections never exceeded 2%. During each experiment the probe temperature was kept constant to within ± 0.2 °C by the passage of dry thermostated air or nitrogen. The overall accuracy of the corrected and normalized excess data is estimated to be better than $\pm 3 \text{ s}^{-1}$.

THEORETICAL BACKGROUND

For a nucleus like oxygen-17, with spin $I = \frac{5}{2}$, the macroscopic magnetization decays, in general, as a weighted sum of three exponentials.⁶ No general analytical expressions exist for the three amplitudes or for the corresponding relaxation rates in terms of the spectral densities characterizing the molecular motion; rather the eigenvalues and eigenvectors of the relaxation matrix must be obtained numerically for each set of values for the spectral densities.

However, in the systems under study the comparatively rapid motion of the 'bound' water and the large fraction of rapidly reorienting bulk water result in an effective spectral density that is only weakly frequency dependent in the experimental frequency range. The relaxation then becomes nearly exponential and approximate analytical expressions for the longitudinal and transverse rates can be derived.^{7,8} For the present data, these expressions are accurate to better than 1%.

Since no ^{17}O quadrupolar splittings were observed for the polyacid solutions, the molecular motion must average the quadrupolar interaction to zero on a time-scale of the order of $1/\chi$, where χ is the quadrupole coupling constant. The relaxation rates can then be expressed as⁶⁻⁸

$$R_1 = \frac{3\pi^2}{625} \chi^2 \left(1 + \frac{\eta^2}{3}\right) [2\tilde{J}(\omega_0) + 8\tilde{J}(2\omega_0)] \quad (1a)$$

$$R_2 = \frac{3\pi^2}{625} \chi^2 \left(1 + \frac{\eta^2}{3}\right) [3\tilde{J}(0) + 5\tilde{J}(\omega_0) + 2\tilde{J}(2\omega_0)] \quad (1b)$$

where ω_0 is the resonance frequency and the reduced spectral density is

$$\tilde{J}(\omega) = \frac{2\tau_c}{1 + (\omega\tau_c)^2} \quad (2)$$

Here it has been assumed that the molecular motion is isotropic, so that the correlation function for the field gradient decays exponentially with a correlation time τ_c . (This assumption will be partly removed in the subsequent treatment). For the H_2^{17}O quadrupole coupling constant we use the recent estimate $\chi = 6.67 \text{ MHz}$,² while the asymmetry parameter is taken to be the same as in ice,⁹ $\eta = 0.925$.

If the ^{17}O nuclei exchange rapidly between two environments or states with different intrinsic relaxation rates but negligible chemical shift difference, then the total rates may be decomposed according to^{10,11}

$$R_i = P_F R_{iF} + P_B R_{iB} \quad (i = 1, 2) \quad (3)$$

where $P_B = nm/55.5$ is the fraction of nuclei in the B state and $P_F = 1 - P_B$. m is the monomer molality and n is the number of motionally perturbed water molecules per monomer. Eqn (3) corresponds to a two-state model with 'free' (F) and 'bound' (B) water. For 'free' water $R_{1F} = R_{2F} \equiv R_F$. 'Rapid exchange' here means that the average 'lifetime' τ_{1B} of a water molecule in the B state is short compared with the intrinsic relaxation times in that state, *i.e.* that $\tau_{1B} \ll 1/R_{1B}$.

Due to the scalar spin-spin coupling between the ^{17}O nucleus and the two protons, the water ^{17}O resonance consists, in the absence of proton exchange, of a triplet¹² with spin-spin coupling constant¹³ $J_{\text{OH}} = 90 \text{ Hz}$. At normal temperatures, however, the proton exchange rate $r > 2\pi J_{\text{OH}}$, making the ^{17}O resonance nearly Lorentzian with a linewidth determined by r , J_{OH} and the transverse relaxation rate, R_2 , in the absence of exchange. In practice, R_2 is obtained from the linewidth at pH values where

$r \gg 2\pi J_{\text{OH}}$, from the proton decoupled linewidth, or from the longitudinal relaxation rate (provided that extreme narrowing conditions obtain).

Starting from the extended Bloch equations,¹² it is straightforward to derive an expression for the ¹⁷O lineshape as a function of r , J_{OH} and R_2 , from which the broadening of the linewidth due to proton exchange,

$$\Delta\nu_{\text{exch}} \equiv \Delta\nu_{\text{obs}} - R_2/\pi,$$

can be obtained numerically. However, for the data presented here, the following simple expression, which is derived in Appendix A, is valid to an excellent approximation

$$\Delta\nu_{\text{exch}} = \frac{4\pi J_{\text{OH}}^2}{r}. \quad (4)$$

The rate of proton exchange in pure water may be written as¹²

$$r_{\text{F}} = \frac{2}{3}k_1[\text{H}_3\text{O}^+] + k_2[\text{OH}^-] \quad (5)$$

where k_1 and k_2 are the second-order rate constants for the acid- and base-catalysed transfer processes, respectively. With $\text{pH} = -\log(\gamma'[\text{H}_3\text{O}^+])$, γ' being an operational activity coefficient, and K_{w} the ionic product of water eqn (5) becomes

$$r_{\text{F}} = \frac{2}{3}k'_1 10^{-\text{pH}} + k'_2 K_{\text{w}} 10^{\text{pH}} \quad (6)$$

where $k'_1 \equiv k_1/\gamma'$ and $k'_2 \equiv \gamma'k_2$.

In an aqueous polyacid solution additional mechanisms for water proton exchange may exist. Let r_{B} be the rate of proton exchange for the fraction P_{B}^{H} of the water molecules which are engaged in proton transfer with prototropic groups on the polymer. [Note that P_{B}^{H} is not necessarily equal to the fraction P_{B} appearing in eqn (3)]. The proton-exchange kinetics is thus described by a six-state model with three spin states for each of the F and B states. However, provided that $P_{\text{B}}^{\text{H}} \ll 1$, the system can be treated as if there were proton exchange between only three (spin) states, with an effective rate

$$r = r_{\text{F}} + \frac{P_{\text{B}}^{\text{H}}}{P_{\text{F}}^{\text{H}}} \left(\frac{1}{r_{\text{B}}} + \tau_{\text{IB}}^{\text{H}} \right)^{-1} \quad (7)$$

where $\tau_{\text{IB}}^{\text{H}}$ is the average lifetime in the B state for the fraction P_{B}^{H} of the water molecules. This result is derived in Appendix B.

RESULTS

In order to determine whether the fast exchange limit is applicable to the water ¹⁷O relaxation in our polyacid solutions, *i.e.* if eqn (3) is valid, we measured the linewidth as a function of temperature in the range 5–93 °C for solutions of PMA at two degrees of dissociation (fig. 1). Under very general conditions, an Eyring plot of $\ln(R_{2,\text{ex}}/T)$ against $1/T$ yields a line of positive slope in the fast exchange limit.¹⁴ This is evidently the case for water interacting with either the coiled ($\alpha = 0.08$) or the extended ($\alpha = 0.54$) conformations (see below) of PMA.

According to eqn (3) the excess relaxation rates may be written as

$$R_{i,\text{ex}} \equiv R_i - R_{\text{F}} = P_{\text{B}}(R_{i\text{B}} - R_{\text{F}}). \quad (8)$$

The evaluation of $R_{i,\text{ex}}$ as described in the Experimental Section is equivalent to setting R_{F} equal to the relaxation rate of pure water (127.3 s^{-1} at 28.0 °C). The excess rates thus include a small contribution ($\lesssim 3 \text{ s}^{-1}$) from sodium and chloride ions (*cf.* Discussion). Fig. 2 shows that the transverse excess relaxation rate is, within the

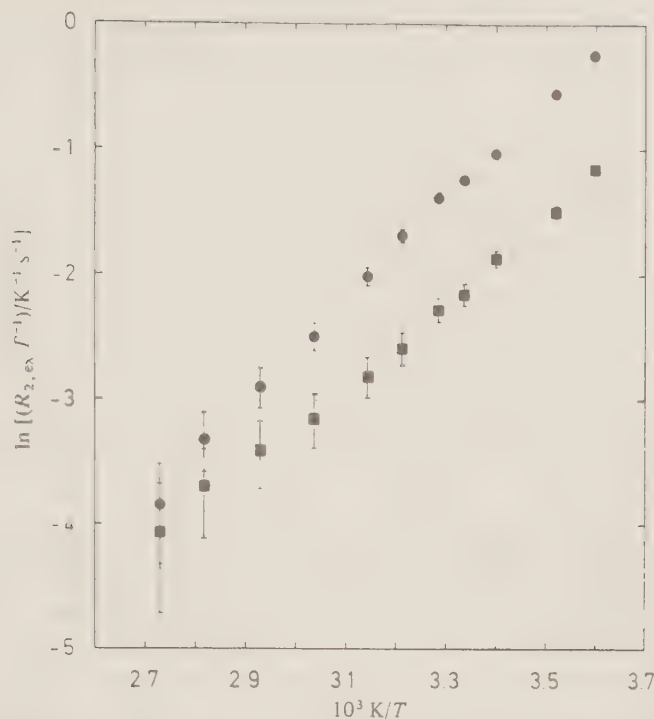


FIG. 1.—Temperature dependence of the ^{17}O transverse excess relaxation rate at 13.56 MHz for 0.55 *m* PMA at $\alpha = 0.08$ (●) and for 0.57 *m* PMA at $\alpha = 0.54$ (■). Error bars correspond to a $\pm 3 \text{ s}^{-1}$ uncertainty in $R_{2, \text{ex}}$.

experimental accuracy, proportional to the monomer molality, except for PMA at $\alpha = 0$. Measurements on PMA at 0.19 and 0.59 *m* as a function of α (table 1) show that this nonlinear behavior becomes less pronounced as the charge density increases, but it persists up to at least $\alpha \simeq 0.2$. In the absence of polymer–polymer interaction, the intrinsic relaxation rates R_{iB} should be concentration independent, whereas P_B and thus, according to eqn (8), $R_{i, \text{ex}}$ should be proportional to the monomer molality. These findings therefore demonstrate the presence of polymer–polymer interaction in PMA solutions at low α in the investigated concentration range.

Note that a linear concentration dependence, as was obtained for PAA and for PMA at $\alpha = 1$, is a necessary, although not sufficient, criterion for absence of polymer–polymer interactions. Indeed, our results show that the ^{17}O relaxation rates in the concentration range $< 0.6 \text{ m}$ are unaffected by *inter*-polymer electrostatic repulsion. Since the nonlinearity for PMA becomes more pronounced with decreasing charge density, it cannot have an electrostatic origin. As an explanation we suggest polymer–polymer association. That this occurs for PMA, but not for PAA (*cf.* also table 2), may be due to stronger van der Waals forces between the PMA chains with their additional methyl groups.

A change in the degree of dissociation of the polyacid may influence the water ^{17}O relaxation directly through the altered charge density or indirectly *via* conformational transitions or changes in counter-ion association. Indeed, fig. 3 reveals a non-trivial α -dependence. For PAA we found that extreme narrowing conditions [$\tilde{J}(\omega) = \tilde{J}(0)$ and thus, according to eqn (1), $R_1 = R_2$] obtain over the entire α range, whereas for PMA at low α values we observed considerable differences between longitudinal and

¹⁷O N.M.R. IN POLYELECTROLYTE SOLUTIONS

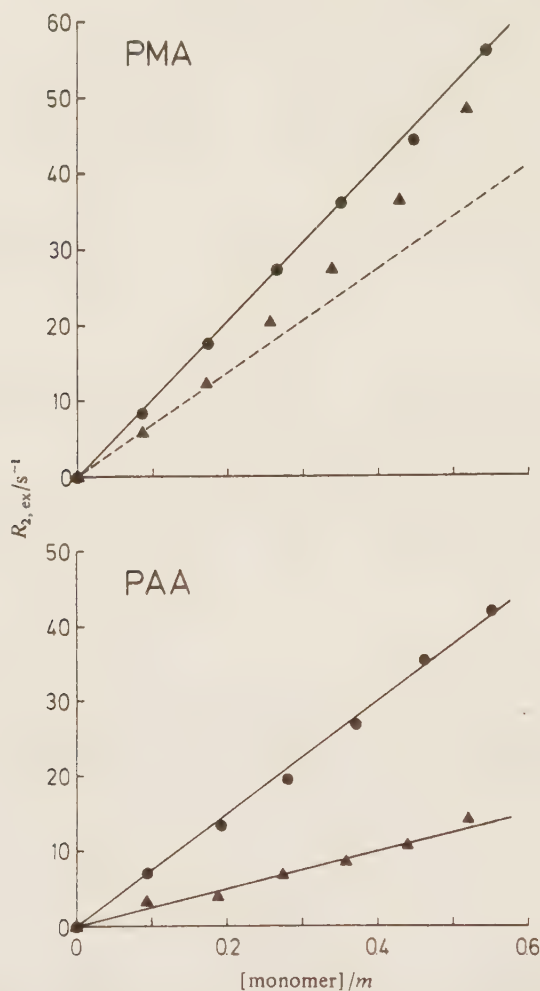


FIG. 2.—Concentration dependence of the ¹⁷O transverse excess relaxation rate at 34.56 MHz and 27.7 °C for aqueous solutions of PAA and PMA at $\alpha = 0$ ($\blacktriangle$) and $\alpha = 1$ ($\bullet$). Solid lines from least-squares fits.

TABLE 1.—RATIO OF NORMALIZED (TO $m = 1$) TRANSVERSE EXCESS RELAXATION RATES AT 13.56 MHz FOR TWO PMA CONCENTRATIONS AT DIFFERENT DEGREES OF DISSOCIATION

α	$\frac{0.19 R_{2,ex}(0.59 m)}{0.59 R_{2,ex}(0.19 m)}$
1.000	1.05
0.222	1.23
0.086	1.39
0.005	1.45
0.000	1.96

Data from the pH range of significant proton exchange broadening, corresponding to $0.3 < \alpha < 1.0$ for 0.19 m PMA, are not included.

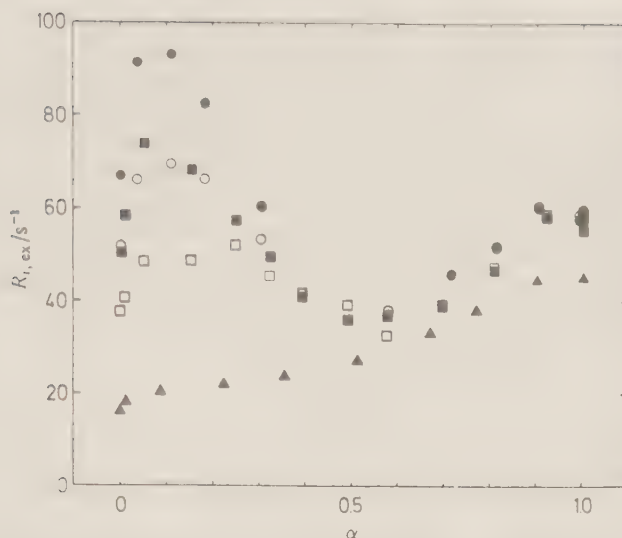


FIG. 3.— ^{17}O excess relaxation rates at 28.0°C plotted against degree of dissociation for 0.59 m PAA ($\blacktriangle$), 0.59 m PMA at 13.56 MHz ($\bullet$, $\circ$), and 0.57 m PMA at 34.56 MHz ($\blacksquare$, $\square$). Open symbols refer to longitudinal, filled symbols to transverse rates. At α values where only filled symbols are shown, measured $R_{1,\text{ex}}$ and $R_{2,\text{ex}}$ overlap. No data from the region of significant proton-exchange broadening are included.

TABLE 2.—EXCESS RELAXATION RATES AT 0.59 m AND 28.0°C FOR MONOMERS AND POLYMERS

monomer	$R_{\text{ex}}^a/\text{s}^{-1}$	polymer	$R_{\text{ex}}^{a,b}/\text{s}^{-1}$
$\text{CH}_3\text{CH}_2\text{COOH}$	10.5	PAA $\alpha = 0$	11.3 ^c
$\text{CH}_3\text{CH}_2\text{COO}^-$	23.6 ^c	PAA $\alpha = 1$	41.2 ^d
$(\text{CH}_3)_2\text{CHCOOH}$	14.4	PMA $\alpha = 0$	^e
$(\text{CH}_3)_2\text{CHCOO}^-$	30.4 ^c	PMA $\alpha = 1$	56.7 ^d

^a The uncertainty in R_{ex} is estimated to be $\pm 2\text{ s}^{-1}$. In all cases $R_1 = R_2$. ^b From the slopes in fig. 2. ^c The contribution of 3 s^{-1} from 0.59 m NaCl or Na^+ (Cl^- makes a negligible contribution) has been subtracted. ^d A contribution of 1 s^{-1} , corresponding to 'free' Na^+ (see Discussion), has been subtracted. ^e Frequency-dependent relaxation rates.

transverse relaxation rates as well as a frequency dependence. This behaviour indicates that there are rapidly exchanging water molecules with motional components on a timescale of nanoseconds. Common to both polyacids is a nearly linear increase in relaxation rates with increasing charge density above $\alpha \simeq 0.5$.

In order to facilitate the interpretation of the ^{17}O relaxation data for PAA and PMA, we studied the corresponding monomers, propionic acid and isobutyric acid, respectively. The results are shown in table 2 together with some polyacid data from fig. 2. The effect of the monomers is more than doubled upon dissociation of the carboxylic group. In the fully protonated state ($\alpha = 0$) PAA produces the same effect as an equivalent concentration of monomers. This is not so for PMA, for which, as noted above, the relaxation rates are frequency-dependent and much larger than for the corresponding monomer solution. In the fully dissociated state ($\alpha = 1$) we observe significantly larger effects from both of the polymers, as compared with the dissociated

monomers. Finally, we note that the difference between PAA and PMA at $\alpha = 1$ is larger than the difference between the anionic monomers.

The broadening of the ^{17}O absorption curve around neutral pH, due to slow water-proton exchange, is drastically reduced on addition of even small amounts of PAA or PMA (fig. 4). This effect is evidence of additional catalytic mechanisms that are much more effective than those operating in bulk water around neutral pH. The shift of the linewidth maximum towards higher pH indicates that dissociation reduces the catalytic efficiency of the polyacid. Furthermore, a reduction of the proton-exchange broadening to the level of the two intermediate, almost coincident, curves requires a 7-fold higher concentration of PMA as compared with PAA. PAA is thus a considerably more powerful proton-exchange catalyst than PMA.

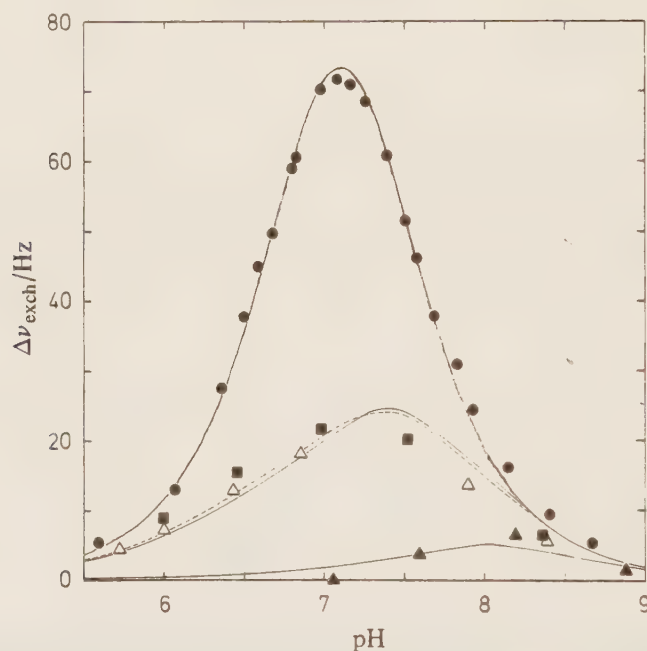


FIG. 4.—Proton-exchange broadening of the ^{17}O resonance plotted against pH at 28.4 °C for H_2O (●), 1.50×10^{-3} M PAA (■, dashed curve), 10.2×10^{-3} M PMA (△) and 0.585 M PMA (▲). The curves are based on least-squares fits to theoretical expressions as explained in the text.

DISCUSSION

GENERAL CONSIDERATIONS

The simplest picture consistent with the temperature and concentration dependences of the water ^{17}O relaxation rate is a fast exchange of water molecules between two states: 'free' (F) and 'bound' (B) water. In attempting a more detailed interpretation one must, even within this relatively simple model, consider several dynamic processes: (1) reorientation of free water molecules, (2) chemical exchange between free and bound states, (3) reorientation (possibly anisotropic) and translation of bound water molecules, and (4) reorientation (possibly anisotropic) of entire polymer molecules (or aggregates) and segments thereof. Furthermore, all these processes may be influenced by the presence of counterions.

To begin with, assume that water molecules in the B state are rigidly bound to the

polyelectrolyte, *i.e.* that processes of type 3 can be disregarded. Furthermore, assume that processes of types 2 and 4 can be described by a single effective correlation time τ_{cB} [*cf.* eqn (10)]. With relaxation rates from fig. 3 for PMA at $\alpha = 0$ and with $\tau_{cF} = 2.35$ ps [from eqn (1) and (2) with $R_F = 127.3 \text{ s}^{-1}$], eqn (1), (2) and (8) yield $\tau_{cB} = 3.3 \pm 1.3$ ns, corresponding to one bound water molecule for every 41 ± 10 monomer units. We regard this as an unreasonably low value for the number of interacting water molecules, even for a relatively compact polymer conformation. (A monolayer coverage of a compact sphere consisting of 90 monomers corresponds to *ca.* 3 water molecules per monomer.)

These considerations led us to refine the model by allowing the bound water molecules some reorientational freedom, while still taking into account the inherent anisotropy of the water-polymer interaction. The local anisotropic reorientation will only partially average the quadrupolar interaction,¹⁵ the remaining part being averaged out by a slower motion, presumably chemical exchange and/or polymer reorientation. Since this extended two-state model involves more parameters than justified by our data, we will introduce several simplifying assumptions: (1) the local and the overall motions occur independently and on different timescales, (2) there is local axial symmetry and (3) the anisotropy is small. The spectral density for the B state may then be decomposed into components associated with the fast (f) and the slow (s) motions^{15, 16}

$$\left(1 + \frac{\eta^2}{3}\right) \tilde{J}_B(\omega) = \left(1 + \frac{\eta^2}{3} - A^2\right) \tilde{J}_{Bf}(\omega) + A^2 \tilde{J}_{Bs}(\omega). \quad (9)$$

Since the fast motion is in the extreme narrowing limit (see below), eqn (2) yields $\tilde{J}_{Bf} = 2\tau_{cB}^f$.

The residual anisotropy A , the magnitude of which is confined to the range $[0, 1]$, is determined by the asymmetry parameter η and by the orientational probability distribution for the 'bound' water molecules with respect to the polymer chain.¹⁶ If the 'bound' water molecules were to reorient completely isotropically, then $A = 0$ giving $\tilde{J}_B = \tilde{J}_{Bf}$, *i.e.* only the fast motion would contribute to the relaxation. From eqn (9), which is valid only for $A^2 \ll 1$, it is seen that for the slow motion to contribute significantly to the relaxation rate, it must be of the order of a factor $1/A^2$ slower than the fast motion. On the basis of water ^{17}O data [ref. (2) and unpublished data] from similar systems, we expect $|A|$ to lie in the range 0.01–0.2.

In the following, we will interpret the direct effect of carboxylic-group dissociation (indirect effects on polymer conformation and counter-ion association will be considered explicitly) on the 'hydration', as measured by the ^{17}O relaxation rate, in terms of variations in reorientational rate and/or anisotropy for a fixed number of water molecules, rather than in terms of a changing 'hydration number'. In view of the short-range character of the water-polyelectrolyte interaction (its most long-ranged component, the average charge-dipole potential, falls off as r^{-4} to first order), we feel that this interpretation is physically reasonable and conceptually preferable. The other view may be more natural in connection with hydration studies through measurement of the water self-diffusion coefficient¹⁷ or of absorption and desorption isotherms.¹⁸ The results from such studies are, however, not simply related to the properties determining water magnetic relaxation rates.

LOW α RANGE

It has been documented with a variety of experimental techniques^{19–29} that PMA, and to a much lesser extent also PAA, in aqueous solution undergoes a conformational transition from an extended form at high α to a more or less compact random coil

at lower α . This transition is undoubtedly the origin of the large ^{17}O relaxation rates for PMA at low α values. The non-linear concentration dependence for PMA (fig. 2 and table 1) implies that, in the investigated concentration range, association occurs also between chain segments situated in different polymer molecules.

At $\alpha = 0$, PAA has the same effect on the ^{17}O relaxation as an equivalent concentration of monomers (table 2). This indicates that the local water reorientation is similar in these two systems and that more extensive motions do not contribute significantly at $\alpha = 0$. For PMA, on the other hand, slow motions must be invoked to explain the much larger effect compared with the monomer solution (table 2), the inequality of R_1 and R_2 , and the frequency dependence (fig. 3). Since the rate and anisotropy of the local water reorientation should be similar for PMA and PAA at $\alpha = 0$, the difference between PMA and its monomer must lie mainly in the slow correlation time τ_{CB}^s . This correlation time can be estimated if we assume that the local water reorientation is the same for PMA as for the monomer, as was found for PAA at $\alpha = 0$. From the data in fig. 3 and table 2 we then find, using eqn (1), (2), (8) and (9), for PMA at $\alpha = 0$: $\tau_{\text{CB}}^s = 6 \pm 2$ ns and $nA^2 = 0.023$. 'Coordination numbers' n in the range 2-10 thus correspond to anisotropies $|A|$ in the range 0.11-0.05.

The maximum in relaxation rates for PMA in the low α range can be understood as the result of two opposing factors. First, deprotonation of carboxylic groups should, through the charge-dipole interaction, increase the anisotropy of the local water reorientation. The factor A^2 in eqn (9) is thereby increased and the slow motion is more heavily weighted, resulting in enhanced relaxation rates with increasing α . Secondly, as the polymer chain gradually unfolds with increasing charge density, the correlation time τ_{CB}^s , which is at least partially (see below) determined by extensive polymer motions, decreases. This is seen from the decreasing ratio $R_{2,\text{ex}}/R_{1,\text{ex}}$ with increasing α in the range 0.1-0.5 (fig. 3). The conformational transition thus has the effect of decreasing the slow motional contribution to the relaxation rates with increasing α .

HIGH α RANGE

Small-angle neutron and X-ray scattering studies of aqueous solutions of PMA²⁵ and PAA,²⁶ respectively, in the concentration range 0.1-0.4 *m* and in the α range 0.4-1.0 have revealed a peak in the plot of scattered intensity against scattering vector. This was taken as evidence for an electrostatically induced lattice-like structure with parallel extended polyelectrolyte chains. Since this ordering was found to persist down to the lowest investigated concentration (*ca.* 0.1 *m*) and degree of dissociation (0.4 and 0.6), the linear dependence of the ^{17}O relaxation rate on concentration at $\alpha = 1$ (fig. 2) and on α above $\alpha \simeq 0.5$ (fig. 3) is not surprising.

Thus, although the ordered structure is a direct result of electrostatic polymer-polymer interaction, this interaction is not expected to affect the water motion as long as the polymer segments remain extended and sufficiently separated.

The monomer data in table 2 clearly demonstrate that the perturbation of the water reorientation, to a large extent, is electrostatically induced. The increase in relaxation rate with increasing α above $\alpha \simeq 0.5$ (fig. 3), where the polyacids exist in an extended conformation,^{19-26, 28} is thus readily accepted. The same situation, with charged residues (carboxylates in particular) contributing more than uncharged ones to the ^{17}O relaxation rate, is found in aqueous protein solutions.² In sharp contrast to our results, deuteron relaxation in PMA solutions³⁰ has been taken as evidence for a decreasing 'hydration' with increasing charge density. Later work^{3, 4} has, however, cast serious doubts on this interpretation. Our results clearly reinforce these doubts. The larger effect on the water ^{17}O relaxation rate of charged groups is *not* a consequence of an increased electric field gradient at the oxygen nucleus. The water

^{17}O field gradient is, to an excellent approximation, of intramolecular origin. Indeed, recent quantum chemical calculations^{2, 16} have shown that the perturbation induced by a nearby charge is negligible.

It remains for us to explain the substantially larger effect on the ^{17}O relaxation rate of the fully dissociated polyacids as compared with the monomers (table 2). One difference between a polyelectrolyte and its separated monomers is that a fraction of the counter-ions associate with the polyelectrolyte, thereby reducing its effective charge density. This phenomenon can often be adequately described in terms of an 'ion condensation' model:^{31, 32} there exists a critical charge density or degree of dissociation, α_c , below which all counter-ions are 'free' and above which all additional counterions become 'bound' to the polyion. For PAA and PMA $\alpha_c = 0.35$, according to this model.

If, in the range $\alpha \gtrsim 0.5$, the polymer (segmental) motions were sufficiently rapid for their contribution to the relaxation rate to be negligible [cf. eqn (9)], then one would expect 'condensed' counter-ions to produce roughly the same effect on the ^{17}O relaxation rate as 'free' counter-ions. We therefore conclude that the much larger effect of the polyacids in the high α range, relative to the monomers, is due to a contribution from slow motions. Consequently, the effect of carboxylic group dissociation on the ^{17}O relaxation rate in the high α range can be viewed as the resultant of three electrostatic contributions. First, the charge-dipole interaction lowers the rate of local water reorientation, *i.e.* increases τ_{CB}^f . This is the sole effect for the monomers. Second, the charge-dipole interaction enhances the anisotropy in the local water reorientation. As noted above, for PAA at $\alpha = 0$ the anisotropy $|A|$ is so small that the slow motion does not influence the relaxation significantly. For charged groups, on the other hand, the anisotropy is sufficiently large for the slow motion to contribute substantially according to eqn (9). Third, association of counter-ions increases the number of water molecules associated with the polyelectrolyte and thus 'feeling' the slow motion. (It has been shown³³ that sodium ions retain their primary hydration sheath upon binding to carboxylate groups.) Finally, it is possible that the aforementioned electrostatic interactions are enhanced in the polyacid solutions because the adjacent hydrocarbon core of the polymer chain reduces the effective local dielectric permittivity through a 'dielectric shielding' effect.³⁴

Table 2 shows that there is a larger difference (15.5 s^{-1}) between PMA and PAA at $\alpha = 1$ than between the anionic monomers (6.8 s^{-1}). In view of the previously discussed lattice-like structure in this α range, it is unlikely that this difference should be caused by the disparity in the degree of polymerization of our polyacid preparations (see Experimental section). As a check, we investigated the molar mass dependence of the ^{17}O linewidth for 0.6 *m* solutions of PAA at $\alpha = 0$ and at $\alpha = 1$. No difference was found between degrees of polymerization 30, 90 and 3200. This leaves us with the conclusion that the additional methyl groups in PMA have a greater effect on the ^{17}O relaxation rate than they have in the monomers. This would be the case if these methyl groups interfere with segmental chain motions, thereby increasing τ_{CB}^s , or if they, by adding to the bulk of the hydrocarbon core, promote the 'dielectric shielding' effect.

Concluding the discussion of relaxation rates, it may be of interest to give an order-of-magnitude estimate of the rate of local water reorientation, *i.e.* of the correlation time τ_{CB}^f . From the monomer data in table 2 we estimate the contribution from a carboxylate group to be *ca.* 17 s^{-1} . Using eqn (1), (2) and (8) we can then calculate the quantity $n(\tau_{\text{CB}}^f - \tau_{\text{CF}})$, where $\tau_{\text{CF}} = 2.35 \text{ ps}$ (see above). In this way we find that 'coordination numbers' n in the range 2-10 correspond to $\tau_{\text{CB}}^f/\tau_{\text{CF}}$ ratios in

the range 7-2. The rate of 'bound' water reorientation is thus less than an order of magnitude slower than in pure water. The same order of magnitude should apply for water associated with the polyacids. In fact, even if we disregard the contribution from slow motions at $\alpha = 1$, we arrive at similar rates. Thus, for PAA at $\alpha = 1$ we find that n values of 2-10 correspond to $\tau_{\text{cB}}^{\text{f}}/\tau_{\text{cF}}$ ratios of 16-4.

PROTON EXCHANGE

In fig 4 is included the result of a redetermination of the rate constants k'_1 and k'_2 appearing in eqn (6). The upper curve, which resulted from a least-squares fit to the complete theoretical expression derived from the extended Bloch equations [the approximate eqn (4) yields identical results], corresponds to $k'_1 = 13.1 \pm 0.3 \text{ dm}^3 \text{ mol}^{-1} \text{ ns}^{-1}$ and $k'_2 = 4.06 \pm 0.1 \text{ dm}^3 \text{ mol}^{-1} \text{ ns}^{-1}$ at 28.4°C . To obtain these values, we have used $J_{\text{OH}} = 90 \text{ Hz}$,¹³ $R_2 = 126 \text{ s}^{-1}$ and $\text{p}K_{\text{w}} = 13.88$.³⁵ Using Arrhenius activation energies³⁶ of 10.9 kJ mol^{-1} (k'_1) and 20.1 kJ mol^{-1} (k'_2), our results can be converted to 25.0°C : $k'_1 = 12.5 \pm 0.3 \text{ dm}^3 \text{ mol}^{-1} \text{ ns}^{-1}$ and $k'_2 = 3.70 \pm 0.1 \text{ dm}^3 \text{ mol}^{-1} \text{ ns}^{-1}$, in close agreement with Meiboom's original results¹² of 10.6 ± 4 and $3.8 \pm 1.5 \text{ dm}^3 \text{ mol}^{-1} \text{ ns}^{-1}$, respectively.

Studying the effect of acetic acid and sodium acetate on the kinetics of proton exchange in aqueous solution by means of the broadening of the proton resonance, Luz and Meiboom³⁷ concluded that the dominant mechanism involves a hydrogen-bonded complex consisting of one undissociated acetic acid molecule and two water molecules. If this mechanism prevails also for the polyacids, an increased polyacid concentration should not only lower the exchange-broadening curve but also shift its maximum towards higher pH. This behaviour is confirmed by our experiments (fig. 4).

On the basis of these observations and the finding (table 2) that the COOH -water interaction is similar in monomer and polymer solutions, we assume that P_{B}^{H} in eqn (7) can be calculated as $2(1-\alpha)m/55.5$, corresponding to two water molecules per undissociated carboxylic group. [In contrast to P_{B} in eqn 3&8, we have included α in the definition of P_{B}^{H}].

The three lower curves in fig. 4 were calculated from least-squares fits to the model defined by eqn (4), (6) and (7). We used α values from separate potentiometric titration experiments and the values given above for J_{OH} , K_{w} , k'_1 and k'_2 . Thus we neglect the influence of counter-ions and added chloride ions on the rate of proton exchange in the F state. According to our studies of the salt effect on the rate of water proton exchange (unpublished data), this influence is completely negligible, at least for the two lower polyacid concentrations. From these data we obtain $(1/r_{\text{B}} + \tau_{\text{FB}}^{\text{H}}) = 5.6 \pm 0.6 \text{ ns}$ for PAA and $31 \pm 5 \text{ ns}$ for PMA. (The less accurate result from the higher PMA concentration is $40 \pm 12 \text{ ns}$.) Previous proton n.m.r. studies at 25°C have resulted in values of 21 ns for acetic acid³³ and $14\text{-}90 \text{ ns}$ for PMA.⁴ The higher catalytic efficiency of PAA, as compared with acetic acid, suggests that another mechanism, presumably involving a chain of one or more water molecules linking a protonated with a deprotonated carboxylate group, contributes to the proton exchange in PAA solutions. This mechanism is expected to be less important for PMA, which was found to be less potent than acetic acid, since the methyl group has a stiffening effect on the polymer chain, as deduced from molecular models.

Although the effect of solutes on the water proton exchange rate has been studied in a variety of systems [e.g. ref. (37) and (4)], no attempt has been made to extract information about the rate of water exchange from the experimental data. However, as shown by the analysis in Appendix B, the experiments yield the composite quantity $(1/r_{\text{B}} + \tau_{\text{FB}}^{\text{H}})$, which constitutes an upper limit for the average residence time $\tau_{\text{FB}}^{\text{H}}$ for those water molecules that exchange protons with the solute.

If the ^{17}O relaxation rate contains a contribution from slow motions, it may be possible to determine the slow correlation time $\tau_{\text{cB}}^{\text{s}}$. If both polymer reorientation (correlation time τ_{rB}) and chemical exchange (average lifetime τ_{1B}) contribute to the slow motion, then this may be characterized by an effective correlation time¹¹

$$\frac{1}{\tau_{\text{cB}}^{\text{s}}} = \frac{1}{\tau_{\text{rB}}} + \frac{1}{\tau_{\text{1B}}}. \quad (10)$$

This result is strictly valid only in the absence of orientational correlation between successive water-polymer encounters.

For PMA at $\alpha = 0$ we found (see above) $\tau_{\text{cB}}^{\text{s}} = 6 \pm 2$ ns. According to eqn (10), this is a lower limit for the water lifetime in state B. Since the effect of PMA on the proton exchange broadening is due mainly, or entirely, to undissociated carboxylic groups, this value may be compared with the upper limit for $\tau_{\text{1B}}^{\text{H}}$ obtained from the proton-exchange broadening. We can therefore conclude that water molecules associated with COOH groups in PMA at $\alpha = 0$ have an average lifetime in the range of 4-36 ns.

SUMMARY

The present study shows that water ^{17}O magnetic relaxation is a valuable tool for the understanding of dynamic processes in aqueous polyelectrolyte solutions. Water molecules associated with the polyelectrolyte are not rigidly bound; rather they reorient anisotropically with a rate that is merely an order of magnitude slower than in bulk water. This perturbation of the water reorientation is, to a large extent, electrostatically induced. Water molecules directly hydrogen-bonded to acidic groups are engaged in rapid proton transfer and have average residence times of the order of 10^{-8} s. In addition, water ^{17}O relaxation rates contain information about polymer dynamics which can be related to results obtained by other techniques.

We are grateful to Maj-Lis Fontell for helping us with the potentiometric titrations and the viscosity measurements and to Hans Gustavsson and Torbjörn Drakenberg for experimental advice and helpful discussions. Grants from Stiftelsen Bengt Lundqvists Minne and from Kungl Fysiografiska Sällskapet i Lund are gratefully acknowledged.

APPENDIX A: EFFECT OF RAPID PROTON TRANSFER ON THE ^{17}O LINEWIDTH

The observed ^{17}O linewidth for pure water at 28 °C is strongly pH dependent with a maximum of *ca.* 115 Hz at pH 7.2 (fig. 4), whereas the 'natural' linewidth (due to quadrupolar relaxation) is merely *ca.* 40 Hz. Despite the considerable magnitude of this proton-exchange broadening, the lineshape remains Lorentzian, or very nearly so. This fact indicates that the proton-exchange broadening can be described, to high accuracy, by an equation which is simpler than the complete lineshape expression. Various limiting forms can be derived by introducing suitable approximations in the exact solution of the extended Bloch equations. Since this involves rather heavy algebra, we will choose a more elegant approach due to Wennerström.¹¹

The essence of Wennerström's treatment of chemical exchange is to write the spin Hamiltonian as

$$H = \sum_i f_i(t) H_i \quad (\text{A } 1)$$

where the sum extends over all states ('sites'). The random functions $f_i(t)$ have the property of being unity if the nucleus considered is in state i at time t and zero otherwise. The ensemble average $\langle f_i(t) \rangle$, which we will denote by $F_i(t)$, is simply the fraction of nuclei in state i at time t . At equilibrium $\langle f_i(t) \rangle_{\text{eq}} \equiv p_i$.

¹⁷O N.M.R. IN POLYELECTROLYTE SOLUTIONS

If the 'natural' linewidth is the same in all states, which, in the present case, must be true since the ¹⁷O field gradient is unaffected by the proton spin state, then it can be shown¹¹ that the exchange broadening is

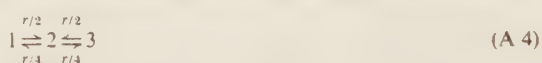
$$\Delta\nu_{\text{exch}} = \frac{1}{2\pi} \int_{-\infty}^{\infty} d\tau \sum_i \sum_j \langle f_i(t) f_j(t+\tau) \rangle_{\text{eq}} \Delta\omega_i \Delta\omega_j \quad (\text{A } 2)$$

where $\Delta\omega_i \equiv \omega_{0i} - \sum_i p_i \omega_{0i}$, ω_{0i} being the resonance frequency in state i . Eqn (A 2) is valid only if the exchange rate is large compared with the relaxation rate and if the lineshape is Lorentzian. Furthermore, it is assumed that the exchange is slow compared with those motions (water reorientation in the present case) that are responsible for the 'natural' linewidth.

The time correlation function in eqn (A 2) may be written⁶ as the product of the probability p_i and the conditional probability $p_{ji}(\tau)$ that the nucleus is in state j at time $t+\tau$, given that it was in state i at time t . Thus

$$\Delta\nu_{\text{exch}} = \frac{1}{2\pi} \int_{-\infty}^{\infty} d\tau \sum_i \sum_j p_i p_{ji}(\tau) \Delta\omega_i \Delta\omega_j. \quad (\text{A } 3)$$

The kinetic scheme for the exchange of ¹⁷O nuclei between different proton spin states is



where r is the proton exchange rate, *i.e.* the inverse of the average lifetime of a water molecule with a given pair of protons. The numerical factors follow from simple probability considerations and the principle of detailed balancing.¹² Furthermore, we have

$$\begin{aligned} p_1 &= \frac{1}{3} & \Delta\omega_1 &= -2\pi J_{\text{OH}} \\ p_2 &= \frac{1}{3} & \text{and } \Delta\omega_2 &= 0 \\ p_3 &= \frac{1}{3} & \Delta\omega_3 &= 2\pi J_{\text{OH}}. \end{aligned} \quad (\text{A } 5)$$

The rate laws for the system (A 4) may be written in matrix notation as

$$\frac{d}{dt} \mathbf{F}(t) = -\mathbf{r} \mathbf{F}(t) \quad (\text{A } 6)$$

where $\mathbf{F}(t)$ is the column vector with elements $F_i(t)$ and

$$\mathbf{r} = r \begin{bmatrix} \frac{1}{2} & -\frac{1}{4} & 0 \\ -\frac{1}{2} & \frac{1}{2} & -\frac{1}{2} \\ 0 & -\frac{1}{4} & \frac{1}{2} \end{bmatrix}. \quad (\text{A } 7)$$

The formal solution to eqn (A 6) is

$$\mathbf{F}(t) = \mathbf{S} \exp(-\lambda t) \mathbf{S}^{-1} \mathbf{F}(0) \quad (\text{A } 8)$$

where $\mathbf{S}$ is the transformation that diagonalizes $\mathbf{r}$ according to

$$\lambda = \mathbf{S}^{-1} \mathbf{r} \mathbf{S}. \quad (\text{A } 9)$$

After a little algebra we find

$$\lambda = r \begin{bmatrix} 1 & 0 & 0 \\ 0 & \frac{1}{2} & 0 \\ 0 & 0 & 0 \end{bmatrix} \quad (\text{A } 10)$$

and

$$\mathbf{S} = \frac{1}{\sqrt{6}} \begin{bmatrix} 1 & -\sqrt{3} & 1 \\ -2 & 0 & 2 \\ 1 & \sqrt{3} & 1 \end{bmatrix}. \quad (\text{A } 11)$$

The conditional probability $p_{ji}(\tau)$ can now be obtained from the solution (A 8) as $F_j(\tau)$, subject to the initial condition $F_k(0) = \delta_{ki}$. Thus

$$p_{ji}(\tau) = \sum_k S_{jk} S_{ki}^{-1} e^{-\lambda_k \tau}. \quad (\text{A } 12)$$

Upon substitution of the elements of λ and S (and its inverse) we find

$$p_{11}(\tau) = p_{33}(\tau) = \frac{1}{2}(e^{-r|\tau|} + 2e^{-r|\tau|/2} + 1) \quad (\text{A } 13)$$

$$p_{13}(\tau) = p_{31}(\tau) = \frac{1}{2}(e^{-r|\tau|} - 2e^{-r|\tau|/2} + 1)$$

where we have introduced absolute values in the exponentials to ensure that the correlation function becomes invariant with respect to time reversal. Conditional probabilities involving state 2 are not needed since $\Delta\omega_2 = 0$. It now remains only to substitute eqn (A 5) and (A 13) into eqn (A 3) and to carry out the integrations. The result is

$$\Delta\nu_{\text{exch}} = \frac{4\pi J_{\text{OH}}^2}{r} \quad (\text{A } 14)$$

In order to assess quantitatively the accuracy of the approximate eqn (A 14), we have compared it with the exact numerical solution of the extended Bloch equations.¹² For given values of r , R_2 and J_{OH} we calculated the exact $\Delta\nu_{\text{exch}}$, which was then inserted into eqn (A 14) to yield an approximate value of r . We used $R_2 = 127.3 \text{ s}^{-1}$ and $J_{\text{OH}} = 90 \text{ Hz}$; however, the result is insensitive to the value of R_2 . Fig. 5 shows that eqn (A 14) is accurate to better than 1% for the polyacid data in fig. 4.

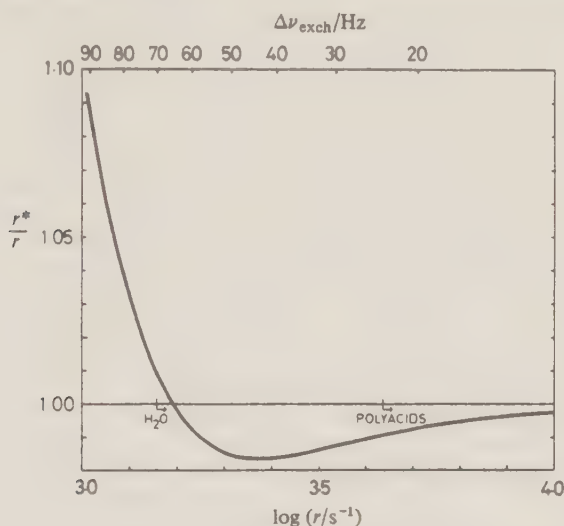
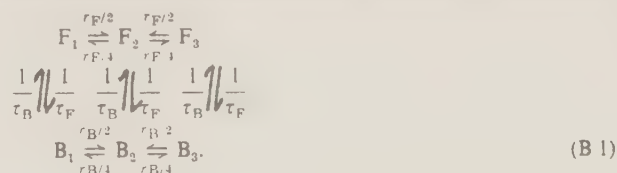


FIG. 5.—Ratio of proton exchange rate, r^* , as calculated by eqn (A 14), to the exact rate r , plotted against $\log r$ and exchange broadening $\Delta\nu_{\text{exch}}$. The ranges of interest for pure water at 28 °C and for the polyacid data in fig. 4 are indicated.

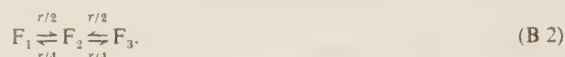
APPENDIX B: EFFECT OF TWO-STATE WATER EXCHANGE ON THE PROTON SPIN-STATE KINETICS

Consider a system in which water molecules can reside in either of two states, defined by their respective proton exchange rates r_F and r_B . At equilibrium, the fraction of water molecules in each state is P_F and P_B , respectively. If the water molecules can exchange between the two states, with rates equal to the inverse of the respective lifetimes τ_F and τ_B , the kinetic scheme for the exchange of ^{17}O nuclei between different proton spin states (indicated by a subscript) is



Assume now that the equilibrium fraction of water molecules in the B state is very small, *i.e.* that $P_B \ll 1$. (For the experimental data to be considered, *i.e.* the two intermediate curves in figure 4, $P_B < 2.5 \times 10^{-4}$.) In the absence of water exchange, the effect of the B state on the observed proton exchange broadening would then be completely negligible. For non-zero water exchange rates, however, the B state can, despite its low population, affect the observed broadening. This is so because a transition between, for example, spin states F_1 and F_2 can occur not only by a proton exchange in the F state, but also *via* two water-exchange events and an intervening proton exchange in the B state. For this latter, indirect, route to contribute significantly to the observed proton spin-state kinetics, the water exchange as well as the proton exchange in the B state must be fast compared with the proton exchange in the F state, *i.e.* $1/\tau_B \gg r_F$ and $r_B \gg r_F$.

It is thus clear that, in the limit $P_B \ll 1$, the only effect of the B states on the proton spin-state kinetics is to increase the effective rate of transitions among the F states. Consequently, the scheme (B 1) reduces to



It remains to derive an expression for the effective proton exchange rate r in terms of P_B , τ_B , r_B and r_F .

The principle of detailed balancing requires that, at equilibrium,

$$\frac{\tau_B}{\tau_F} = \frac{P_B}{P_F} = \frac{B_1 + B_2 + B_3}{F_1 + F_2 + F_3} \quad (\text{B } 3)$$

where the F_i and B_i denote fractional populations. Furthermore, from the rate laws pertaining to scheme (B 1) we find that, at equilibrium

$$\frac{dB_1}{dt} = 0 = \frac{1}{\tau_F} F_1 - \left(\frac{r_B}{2} + \frac{1}{\tau_B} \right) B_1 + \frac{r_B}{4} B_2 \quad (\text{B } 4)$$

$$\frac{dB_3}{dt} = 0 = \frac{1}{\tau_F} F_3 - \left(\frac{r_B}{2} + \frac{1}{\tau_B} \right) B_3 + \frac{r_B}{4} B_2. \quad (\text{B } 5)$$

Combination of eqn (B 3)-(B 5) leads to

$$B_2 = \frac{P_B \tau_B / 2 (F_1 + F_2 + F_3) + 1/r_B F_2}{(1/r_B + \tau_B)}. \quad (\text{B } 6)$$

Consider now the return from an infinitesimal displacement of the equilibrium population of the species F_2 . According to the scheme (B 1)

$$\frac{dF_2}{dt} = \frac{r_F}{2} F_1 - \left(\frac{r_F}{2} + \frac{1}{\tau_F} \right) F_2 + \frac{r_F}{2} F_3 + \frac{1}{\tau_B} B_2. \quad (\text{B } 7)$$

Since the actual populations are assumed to differ only infinitesimally from their equilibrium values, we may substitute B_2 from eqn (B 6) into eqn (B 7) to obtain

$$\frac{dF_2}{dt} = \frac{1}{2} \left[r_F + \frac{P_B}{P_F} \left(\frac{1}{r_B} + \tau_B \right)^{-1} \right] (F_1 - F_2 + F_3). \quad (\text{B } 8)$$

According to the equivalent scheme (B 2)

$$\frac{dF_2}{dt} = \frac{r}{2} (F_1 - F_2 + F_3) \quad (\text{B } 9)$$

which, on comparison with eqn (B 8), yields the desired result

$$r = r_F + \frac{P_B}{P_F} \left(\frac{1}{r_B} + \tau_B \right)^{-1}. \quad (\text{B } 10)$$

Eqn (7) in the main text differs slightly in notation.

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V

Protein Hydration from Water Oxygen-17 Magnetic Relaxation

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Abstract: Water oxygen-17 magnetic relaxation is shown to be a powerful technique for studying protein hydration. Longitudinal and transverse ^{17}O relaxation rates were measured at variable frequency (4–35 MHz), temperature, pH, and protein concentration in aqueous solutions of seven proteins. The data were analyzed in terms of a fast exchange two-state model with local anisotropy. A water ^{17}O quadrupole coupling constant of 6.67 MHz and an order parameter of 0.06 (from ^{17}O splittings in lyotropic liquid crystals) results in approximately two layers of hydration water having a reorientational rate less than 1 order of magnitude slower than that of bulk water. This rapid local motion has a small anisotropic component, which is averaged out by protein reorientation with a correlation time of the order of 10 ns. Due to electrostatic protein–protein interaction the protein reorientation is considerably slower than predicted by the Debye–Stokes–Einstein equation. Charged residues, particularly carboxylate, are more extensively hydrated than other residues, accounting for the variation in the extent of hydration between different proteins.

Introduction

Despite the multitude of experimental techniques that have been used to study protein hydration,^{1–3} a consistent picture of the structural and dynamical details of the protein–water interaction has still not emerged. Thus, it is worthwhile to search for new

techniques to study the interacting water molecules as directly as possible.

To determine whether water ^{17}O magnetic relaxation is such a method, we have measured longitudinal and transverse ^{17}O

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relaxation rates over a decade of resonance frequencies in aqueous solutions of seven proteins. (^{17}O relaxation rates in protein solutions have been reported in four previous studies. In two⁴⁻⁵ of these the ^{17}O data alone did not yield any quantitative conclusions, whereas the other two^{6,77} are concerned with specific interactions between water and protein-bound metals.)

Compared to proton and deuteron magnetic relaxation, which have been used extensively in protein hydration studies,^{4,6-11} ^{17}O relaxation has at least four important advantages: (i) the strong quadrupolar interaction leads to large relaxation effects, thus permitting studies at reasonably low protein concentrations; (ii) the intramolecular origin of the electric field gradient at the water oxygen nucleus makes the quadrupolar interaction virtually independent of the molecular environment, which greatly facilitates the interpretation of relaxation data; (iii) except for a narrow pH range around neutral, the ^{17}O relaxation is not influenced by proton (deuteron) exchange with prototropic residues on the protein, which is a serious problem in ^1H and ^2D relaxation,^{12,37} but can only be affected by exchange of entire water molecules (the ^{17}O -exchange broadening around neutral pH may be eliminated through proton decoupling¹³); (iv) cross-relaxation, which contributes significantly to ^1H relaxation,⁷¹ is unimportant for ^{17}O .

Experimental Section

Materials. Human plasma albumin (HPA) was obtained from AB KABI, Stockholm, as a freeze-dried preparation (batch no. 50412) and was used without further purification. HPA solutions were prepared by weight, assuming 95% purity.⁵⁹

Horse heart cytochrome *c* (cyt *c*) was prepared by the method of Margoliash and Walasek¹⁴ and further purified on an ion-exchange resin to separate deamidated forms from the native protein (the result was checked by gel electrophoresis). Reduced cyt *c* was prepared by ascorbate reduction and salt removed by dialysis. For the measurements on D_2O solutions, the protein was lyophilized and redissolved in D_2O .

Human (adult) oxyhemoglobin (Hb) was prepared by the ammonium sulfate method¹⁵ and deionized on an ion-exchange column.

Parvalbumin (PA), $pI = 4.25$, from carp muscle (*Cyprinus carpio*) was isolated by the method of Pechère et al.¹⁶ and stored as lyophilized powder.

Hen egg white lysozyme (Lyz), grade 1, was purchased from Sigma Chemical Co. as lyophilized powder and was used without further purification.

Horse liver alcohol dehydrogenase (ADH), apoenzyme with the two catalytic Zn^{2+} ions removed, was a gift from Dr. Inger Andersson. The protein was prepared by the method of Maret et al.¹⁹

Human (polyclonal) immunoglobulin G was a gift from Dr. C. Borrebaeck, Biochemistry 2, Chemical Center, Lund, Sweden.

Protein concentrations (except HPA) were determined spectrophotometrically by using $\epsilon^{550} = 29.5 \text{ cm}^{-1} \text{ mM}^{-1}$ (ferro cyt *c*),¹⁸ $a^{541} = 0.85 \text{ cm}^{-1} \text{ mg}^{-1} \text{ mL}$ (Hb),¹⁵ $\epsilon^{259-269} = 1000 \text{ cm}^{-1} \text{ mM}^{-1}$ (PA),¹⁷ $a^{280} = 2.65 \text{ cm}^{-1} \text{ mg}^{-1} \text{ mL}$ (Lyz),¹⁸ $a^{280} = 0.45 \text{ cm}^{-1} \text{ mg}^{-1} \text{ mL}$ (ADH),¹⁹ $a^{280} = 1.32 \text{ cm}^{-1} \text{ mg}^{-1} \text{ mL}$ (IgG).¹⁸

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All protein solutions were made from doubly distilled (quartz apparatus) water or 99.7 atom % D_2O (Ciba-Geigy) and used within 24 h of preparation. H_2O or D_2O enriched to 10 atom % in ^{17}O (Biogenzia Lemania, Lausanne) was added to obtain protein solutions with ca. 1 atom % ^{17}O . pH (pD) was adjusted with HCl and KOH (DCl and KOD). For the HPA solutions we used KCl (Suprapur, Merck).

pH measurements were made with a Radiometer PHM 52 instrument equipped with a GK 2322C combination electrode. For the potentiometric titration (HPA in D_2O) we used a thermostated titration vessel with nitrogen atmosphere and a microburette. Conversion to pD values was made according to²⁰ $pD = pH^* + 0.45$, where pH^* is the instrument reading for a D_2O solution with the electrode calibrated in standard H_2O buffers.

Relaxation Measurements. Oxygen-17 relaxation rates were measured at four frequencies: (i) at 34.565 MHz on a home-built Fourier-transform spectrometer equipped with a 6 T magnet (Oxford Instrument Co. Ltd.), (ii) at 13.564 MHz on a modified Varian XL-100-15 Fourier-transform spectrometer using an external proton lock, (iii) at 8.256 and 3.994 MHz on a Bruker BKR-322s spectrometer with a Varian V-71 computer using a home-made interface and program. Longitudinal relaxation rates were measured by inversion recovery ($\pi - \tau - \pi/2$ pulse sequences). Transverse relaxation rates were obtained from the line width $\Delta\nu_{\text{obsd}}$ at half-height of the absorption curves according to $R_{2,\text{obsd}} = \pi\Delta\nu_{\text{obsd}}$, except at the two lowest frequencies where the Carr-Purcell-Meiboom-Gill sequence was employed. At least three separate measurements were made for each data point. The probe temperature was kept constant within 0.2 °C by passage of dry thermostated air or nitrogen. We used sample tubes with an outer diameter of 12 or 8 mm (Bruker). The nonlinear fits of the dispersion data were made with a modified Marquadt algorithm.²¹

Proton-Exchange Broadening. Around neutral pH the water proton exchange is sufficiently slow to produce a broadening of the ^{17}O absorption peak.⁶⁹ At 27 °C the pH dependence of the line width in H_2O is almost symmetrically peaked around pH 7.2, where the exchange broadening amounts to ca. 70 Hz. The ^{17}O dispersion data were obtained from protein solutions with pH at least 1.8 units from the maximum; the broadening is then less than 2 Hz and may be corrected with the help of pure H_2O data. Due to additional catalytic mechanisms for proton exchange in the presence of prototropic side chains, the real exchange broadening correction is always smaller than for pure H_2O . Data points around neutrality are therefore uncertain and have been omitted (Figure 7). The smaller magnetic moment of the deuteron (compared to the proton) results in a smaller exchange broadening in D_2O (12 Hz maximum at pD 7.6). This is the reason that some of the experiments reported here were done on D_2O solutions.

Results

Relaxation Theory. The relaxation theory for the oxygen-17 nucleus is complicated by the large spin quantum number $5/2$. If the molecular motion causing quadrupolar relaxation has components with correlation times of order of the inverse resonance frequency $1/\omega_0$ or longer, i.e., if in its spectral density $J(0) \neq J(\omega_0)$ (so-called "nonextreme narrowing" conditions), then the relaxation must be described by a sum of three decaying exponentials.^{22,28}

If the ^{17}O nucleus exchanges between environments with different intrinsic relaxation rates, even more exponentials are needed to describe the decaying nuclear magnetization. For the important case of fast exchange, i.e., when the exchange rates exceed the intrinsic relaxation rates, the relaxation matrix **R** may be decomposed according to²³ eq 1, where the sum runs over all environments ("states") *S* and *P_S* is the fraction of nuclei in state *S*.

$$\mathbf{R} = \sum_S P_S \mathbf{R}_S \quad (1)$$

For spin $5/2$ it is not possible to obtain general analytical expressions for the decay of the longitudinal and transverse magnetization, but numerical computations²⁴ for a two-state model

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with one state (bulk water in this case) under "extreme narrowing" conditions show that the longitudinal magnetization decays as a single exponential in all cases of practical interest, while the transverse magnetization, under similar conditions, decays as a sum of three exponentials. However, since the preexponential factors depend on the distribution of nuclei over different sites as well as on the corresponding correlation times²⁴ the transverse magnetization will also decay exponentially for $P_S \lesssim 0.1$ and $\tau_c \lesssim 50$ ns. In fact, in the experiments reported here the dominating exponential always exceeds 0.99 relative amplitude (except for the most concentrated HPA solutions in Figure 5, where it was 0.95 for R_2 at the highest frequency, and for the highest L_{yz} and HPA concentrations in Figure 6, where it was 0.8 for R_2 at 13.564 MHz).

For a fast exchange two-state model we may thus write the excess relaxation rates as

$$R_{i,ex} \equiv R_{i,obsd} - R_{ref} = P_{PR}(R_{i,PR} - R_{ref}) \quad (i = 1, 2) \quad (2)$$

where $R_{i,obsd}$ is the observed relaxation rate in a protein solution, R_{ref} is the relaxation rate in pure water of the same temperature, and the mole fraction P_{PR} and relaxation rates $R_{i,PR}$ refer to those water molecules that interact detectably with the protein, i.e., the "hydration water" in the ^{17}O relaxation sense.

Since the experimental data could not be fitted to a simple two-state fast exchange model (two parameters), in which the hydration water is described by a single correlation time, we introduced the three-parameter model described in the following. Protein-water interactions are inherently anisotropic on a time scale that is long compared to the reorientational time of the hydration water.⁷³ The averaging of the quadrupolar interaction is therefore most conveniently treated as a two-step process.^{25,26} In the first step a fast, slightly anisotropic, reorientational motion partially averages the quadrupolar interaction, while in the second step the remaining part of the quadrupolar Hamiltonian is averaged to zero by a slower process, which may consist of protein reorientation, internal motion of protein segments, translational diffusion of water molecules along the protein surface, or water exchange between the hydration region and the bulk. Since no quadrupolar splittings are observed, this slower motion must have a correlation time no longer than the inverse quadrupole coupling constant, i.e., ca. 100 ns.

A detailed analysis^{25,26} shows that the quadrupolar Hamiltonian, as well as the correlation functions and spectral densities, can be divided into two terms corresponding to the independent fast and slow motions, respectively. Equation 2 then reads

$$R_{i,ex} = P_{PR}(R_{i,f} + R_{i,s} - R_{ref}) \quad (i = 1, 2) \quad (3)$$

We now assume that there is axial symmetry⁷⁰ around the local director (normal to the protein surface) and that the correlation functions are exponential. The latter approximation is reasonable if the local anisotropy of the fast motion is small and if any reorientational motion contributing to the long correlation time is nearly isotropic. An approximation of this kind, although not required for the general conclusions, is convenient for the physical interpretation of the dynamical information. If, furthermore, the fast motion is under "extreme-narrowing" conditions in the investigated frequency range (i.e., if $\tau_f \lesssim 1$ ns), then the two contributions to the excess relaxation rates become²⁵⁻²⁹

$$R_f = (12\pi^2/125)(1 + \eta^2/3 - S^2)\chi^2\tau_f \quad (4a)$$

$$R_{i,s} = (12\pi^2/125)(S\chi)^2 f_i(\tau_s, \omega_0) \quad (i = 1, 2) \quad (4b)$$

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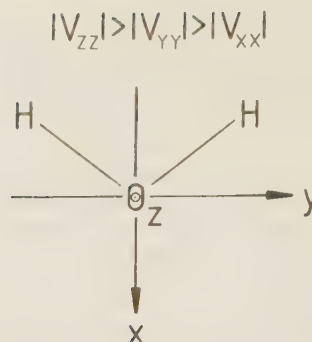


Figure 1. Principal axes system for the electric field gradient tensor at the oxygen nucleus in H_2O .

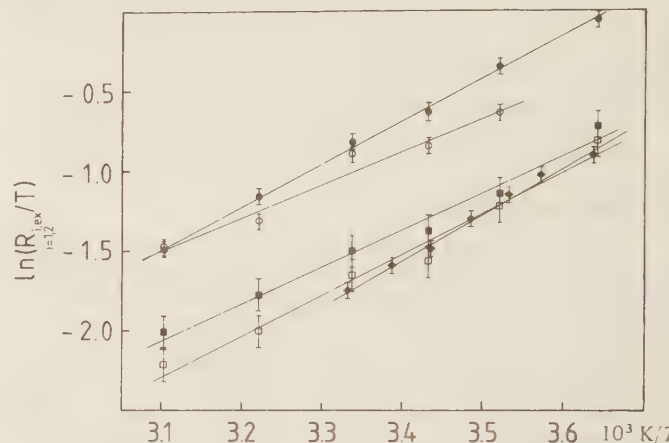


Figure 2. Temperature dependence of the ^{17}O excess longitudinal and transverse relaxation rates for D_2O solutions containing oxidized ($R_{2,ex}$ (●), $R_{1,ex}$ (■)) and reduced ($R_{2,ex}$ (○), $R_{1,ex}$ (□)) cyt *c* and HPA ($R_{2,ex}$ (◆)). Measurements were made on 5 mM cyt *c* at pH 9.9 and 2.85×10^{-4} M HPA at pH 5.3. Error bars are based on estimated uncertainties in line width measurements (R_2) or standard deviation from inversion recovery semilog plot (R_1).

(R_f of course, becomes frequency dependent at sufficiently high frequencies). In eq 4 τ_f and τ_s are the correlation times for the fast and slow motions, respectively, and $\chi \equiv |eQV_{zz}/h|$ is the quadrupole coupling constant. The general form of the functions $f_i(\tau_s, \omega_0)$ is not known; they were computed numerically²⁴ in the process of diagonalization of the total relaxation matrix. The local "order parameter" S is given by^{25,30} eq 5, where the S_{ii} are diagonal

$$S = S_{zz} + (\eta/3)(S_{xx} - S_{yy}) = \frac{(1/2)[(3 \cos^2 \theta - 1) + \eta \sin^2 \theta \cos 2\phi]}{(5)}$$

components of the traceless orientation tensor S for the water molecule, expressed in the principal axes system of the electric field gradient tensor V (Figure 1). The asymmetry parameter for the field gradient is defined as $\eta \equiv (V_{xx} - V_{yy})/V_{zz}$, V_{ii} being components of the electric field gradient at the ^{17}O nucleus expressed in the principal axes system of Figure 1. θ and ϕ are the polar and azimuthal angles, respectively, of the maximal field gradient component V_{zz} with respect to the local director. The averages in eq 5 are to be taken over a time that is long compared to the correlation time τ_f for the fast motion.

Temperature Dependence. To determine whether the fast exchange limit is applicable for the hydration water, i.e., if eq 1 and 2 are valid, we measured relaxation rates as functions of temperature for HPA and cyt *c* (at two pH values). It can be shown under very general conditions that an Eyring plot of $\ln(R_{i,ex}/T)$ vs. $1/T$ yields a line of positive slope in the fast exchange limit.³¹

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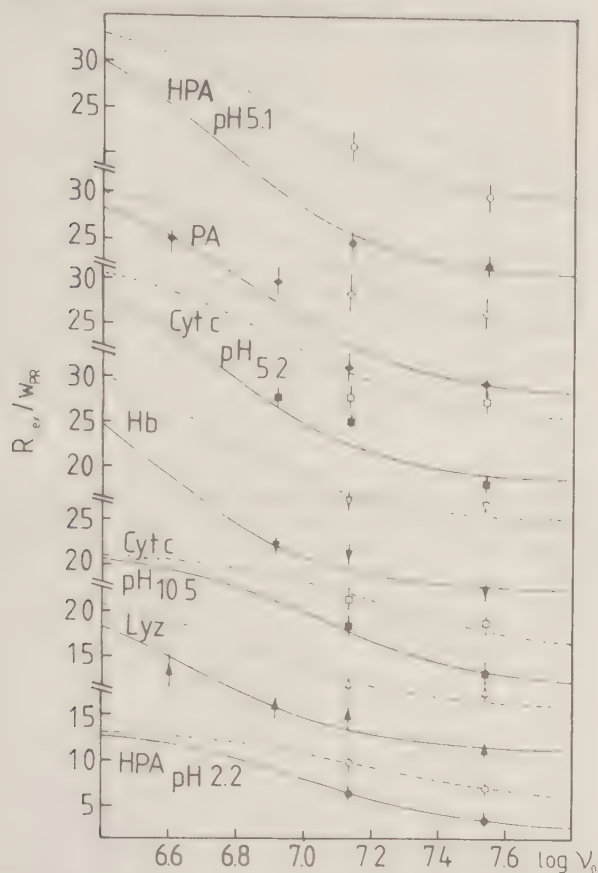


Figure 3. Dispersion of the ^{17}O excess longitudinal (filled symbols, solid curves) and transverse (open symbols, dashed curves) relaxation rates normalized to unit protein concentration w_{PR} (mass %) for aqueous protein solutions at 27.0 °C (28.7 °C for HPA). Concentrations and pH values are listed in Table I. The curves were calculated as explained in the text. Error bars are as in Figure 2.

As seen from Figure 2 this is the case for the investigated protein solutions. (Due to the complicated temperature dependence no simple activation parameter can be extracted from the plot.³²) According to eq 2 and P_{PR} values from Table I the fast exchange criterion $\tau_{ex} \ll 1/R_{2,PR}$ implies that the average residence time for a water molecule in the hydration region is shorter than ca. 0.1 ms.

Frequency Dependence. Oxygen-17 relaxation rates in aqueous protein solutions are frequency dependent in the range 4–35 MHz, demonstrating that the relaxing motions include a component with correlation time on the order of 10 ns. The “dispersion” of the longitudinal and transverse excess relaxation rates for seven protein solutions is shown in Figure 3. The data were fitted to the model defined by eq 3 and 4 with the three independent parameters $[P_{PR}X^2((1 + \eta^2/3 - S^2)\tau_f - \tau_{ref})]$, $[P_{PR}(SX)^2]$ and τ_s . (Actually, the fit was made with τ_f in eq 4a replaced by $f_1(\tau_f, \omega_0)$, but it was found that the fast component R_f is under “extreme-narrowing” conditions in the frequency range studied. Thus, it is not possible to separate $[P_{PR}X^2(1 + \eta^2/3 - S^2)]$ from τ_f as for the slow component.)

At first glance, the data in Figure 3 may appear insufficient to determine the theoretical curves. However, it should be realized that the two curves are not independent and that a separation of the fast and slow relaxation contributions does not require data from the dispersion region (where $R_{i,ex}$ is frequency dependent), since $R_{2,ex}$ (at all frequencies) contains information about the slow component through the spectral density at zero frequency. From Figure 4, which illustrates the dispersion behavior expected from our model over a larger frequency range in order to include the high- and low-frequency limits of the slow component, one can see that it is sufficient to determine the high-frequency plateau

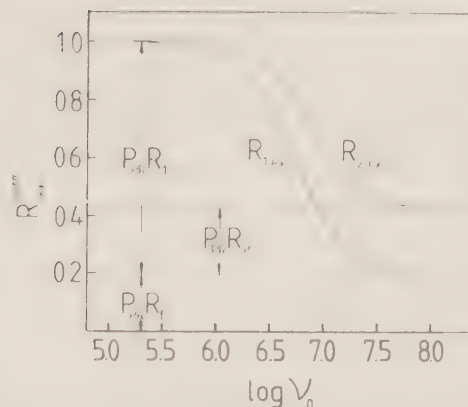


Figure 4. Dispersion of the (normalized) ^{17}O excess relaxation rates showing the limiting behavior and the definition of the slow (low-frequency limit) and fast contributions. In calculating the curves typical values of the three parameters were used.

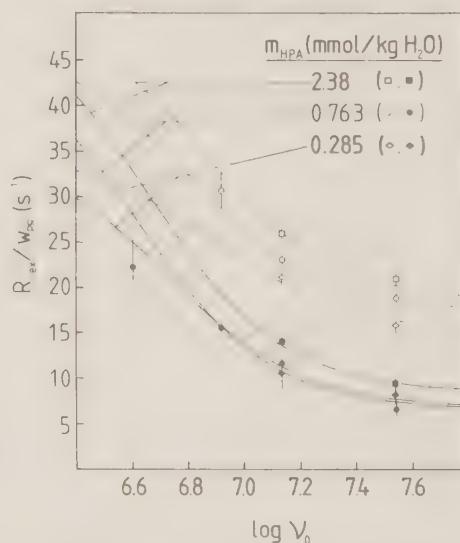


Figure 5. Dispersion of the ^{17}O excess relaxation rates normalized to unit protein concentration w_{PR} (mass %) for aqueous HPA solutions at pH 5.16 $\pm$ 0.08. The intermediate concentration was studied at 27.0 °C and the other two at 28.7 °C. The curves (longitudinal, solid; transverse, dashed) were calculated as explained in the text. Error bars are as in Figure 2.

to obtain the two quantities $P_{PR}R_f$ and $P_{PR}R_d$ measuring the fast and slow contributions, respectively.

The dispersion from HPA solutions at three concentrations is shown in Figure 5. The difference in the (normalized) data is partly due to the temperature difference, but effects of protein-protein interaction are also apparent (cf. next section).

The results of fitting the data in Figures 3 and 5 are given in Table I. From the standard deviations of the fits we estimate uncertainties of ca. 20% in the two composite parameters and 10–50% in τ_s (the larger uncertainties here reflect the poor low frequency data). In the limit of exponential relaxation described by second-rank tensors²⁸ the ratio $R_d/R_{1,s}$ should equal 0.3. From the fitted parameters we calculated this ratio (Table I) as a test of consistency of the data.

Protein Concentration Dependence. Figure 6 shows the dependence of the ^{17}O transverse relaxation rate on protein concentration for aqueous solutions of lysozyme and human plasma albumin. It is seen that the excess relaxation rate increases linearly up to protein concentrations between 5 and 10%, whereas at still higher concentrations it increases faster than linearly. This behavior is also apparent from Figure 5.

pD Dependence. The pD dependence of the ^{17}O relaxation was studied for D₂O solutions of HPA and IgG; the results are shown in Figure 7. The curves represent the total number of charged residues on the protein. For HPA (Figure 7a), we obtained this

Table I. ^{17}O Relaxation Data for Aqueous Protein Solutions

sample ^a	pH	w _{PR} , mass %	m _{PR} , mmol/kg	R_1 , ex/w _{PR} at 13.56 MHz, s ⁻¹	$P_{\text{PR}}^{\text{X}^2}$, [(1 + $\eta^2/3 - S^2$) τ_f] s ⁻¹	$P_{\text{PR}}^{\text{X}^2}$, - τ_{ref} , s ⁻¹	$10^3 P_{\text{PR}}$	$H_2\text{O}/100$ g of PR	τ_f , ps	τ_s , ns	τ_g/τ_{rot} ⁽²⁾ b	mean center- to-center distance in units of diameter of gyration ^b
parvalbumin, pI 4.25	8.99	2.40	2.15	19.5	21.6	4.50	2.2	88	20	13	4.4	3.8
cytochrome c, ferri	5.22	5.00	4.25	17.0	41.1	8.07	3.9	74	21	16	6.6	3.3
	10.49	5.00	4.25	16.5	36.6	9.37	4.5	86	17	8		3.3
lysozyme	5.11	8.29	6.31	12.2	44.3	7.89	3.8	43	23	19	4.6	2.3
hemoglobin, oxy	9.17	4.78	0.779	16.2	34.0	5.47	2.6	53	25	25	1.9	2.9
plasma albumin ^c (0.15 M KCl)	5.09	1.86	0.285	21.0	13.6	3.34	1.6	85	17	16	0.4	2.7
alcohol dehydrogenase, apo (0.15 M KCl, 25 mM MES)	2.18	1.86	0.285	9.9	4.65	2.42	1.2	62	9	9		2.7
immunoglobulin G, polyclonal (0.15 M KCl, D ₂ O)	5.24	4.83	0.763	23.0	33.8	9.74	4.7	93	15	21		2.0
	5.11	13.7	2.38	25.8	123	31.9	15	98	16	19		1.4
	5.73	3.5	0.46	34.0								2.6
	6.0	0.77	0.054	39.0								>3

^a The medium was H₂O and the temperature 27.0 °C unless otherwise stated. See also Experimental Section. ^b See Table II. ^c All albumin data, except at pH 5.24, refer to 28.7 °C.

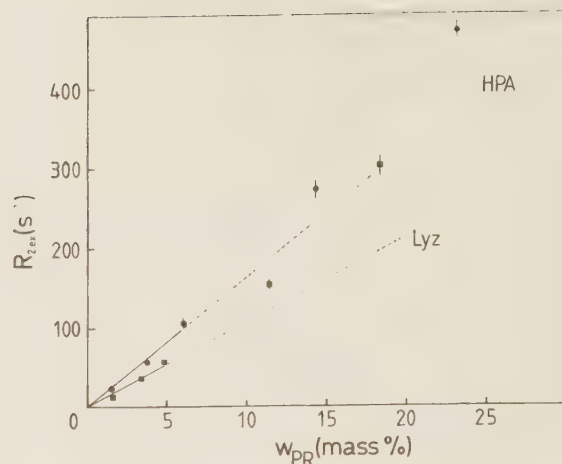


Figure 6. Protein concentration dependence of the ^{17}O excess transverse relaxation rate (at 13.56 MHz) for aqueous solutions of Lyz (pH 5.1) and HPA (pH 5.2) at 28.5 °C. The lines were drawn as an aid to the eye.

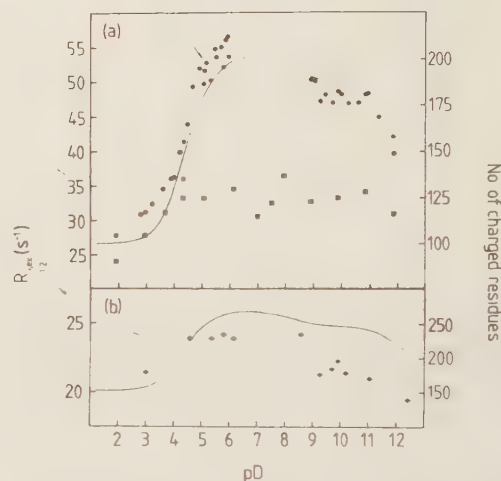


Figure 7. Variation of ^{17}O excess longitudinal (■) and transverse (●, ◆) relaxation rates (13.56 MHz) with pD at 28.0 °C for D₂O solutions containing (a) 2.75×10^{-4} M HPA (0.15 M KCl) and (b) 5.4×10^{-5} M IgG. The data point marked with an arrow was obtained by reverse titration from pD 2. The curves giving the number of charged residues were constructed according to the text.

quantity from a potentiometric titration in 0.15 M KCl/D₂O. The data treatment as well as the number and identity of prototropic groups were the same as in ref 33. The pK_D values so obtained closely agree with previously determined³³ pK_H values corrected for the solvent isotope effect.³⁴ The curve for IgG (Figure 7b) was calculated from the amino acid composition³⁵ (assuming that all prototropic residues are accessible for titration) and pK values typically found in proteins³⁶ corrected for the solvent isotope effect.³⁴ Figure 7 reveals a correlation between the number of charged residues and ^{17}O relaxation rate, particularly for the carboxylate groups.

Discussion

The Quadrupole Coupling Constant. To separate the quantities P_{PR} , S , and τ_f entering the composite fitted parameters, it is desirable to have an accurate value for the water ^{17}O quadrupole

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coupling constant χ . This quantity may be obtained from the ^{17}O relaxation rate in pure water, which is given by²⁸ eq 6, provided

$$R = (12\pi^2/125)\chi^2(1 + \eta^2/3)\tau_{\text{rot}}^{(2)} \quad (6)$$

that an independent estimate of the second-rank rotational correlation time $\tau_{\text{rot}}^{(2)}$ is available. (Here we assume that the ^{17}O quadrupolar relaxation in pure water may be described by a single correlation time.³⁸)

The standard procedure is to use dielectric relaxation data, from which the first-rank rotational correlation time $\tau_{\text{rot}}^{(1)} = 3\tau_{\text{rot}}^{(2)}$ may be extracted. To obtain $\tau_{\text{rot}}^{(1)}$ from the measured macroscopic dielectric relaxation time τ_{diel} , it is necessary to apply a correction. The exact form of this correction has been a controversial issue, but the most reliable relation is now considered to be³⁹

$$\tau_{\text{rot}}^{(1)} = \tau_{\text{diel}} K^{-1/(2K+1)} \quad (7)$$

where $K \equiv \epsilon_s/\epsilon_\infty$, ϵ_s being the static relative permittivity and ϵ_∞ the same quantity in the high-frequency limit.

From a large number of measurements on different samples using different pulse sequences on several spectrometers, we have determined the ^{17}O relaxation rates $R(\text{H}_2\text{O}) = 131.0 \pm 2.0 \text{ s}^{-1}$ and $R(\text{D}_2\text{O}) = 167.4 \pm 2.0 \text{ s}^{-1}$ at 27.0 °C in the absence of exchange broadening. Using $\tau_{\text{diel}} = 7.79 \text{ ps}$, $\epsilon_s = 77.85$, and $\epsilon_\infty = 4.21$ (obtained from a computer fit to dielectric data from seven different studies⁴⁰) for H_2O at 27.0 °C and $\tau_{\text{diel}} = 10.03 \text{ ps}$, $\epsilon_s = 77.23$, and $\epsilon_\infty = 4.0$ for D_2O ⁴¹ at 27.0 °C in combination with the above-mentioned ^{17}O relaxation rates, we get from eq 6 and 7: $\chi(1 + \eta^2/3)^{1/2} = 7.58 \text{ MHz}$ for H_2O and 7.56 MHz for D_2O . The excellent agreement is consistent with the similar electron distribution and hydrogen (deuteron) bond geometry in H_2O and D_2O . Based on the estimated uncertainties in the ^{17}O relaxation rates, a 1% uncertainty in τ_{diel} , and a 5% uncertainty in the dielectric

correction, we get an uncertainty of ± 0.20 in the effective quadrupole coupling constant. The asymmetry parameter is assumed to be the same as in ice, i.e., $\eta = 0.93$ for both H_2O ⁷⁸ and D_2O .⁴² With this value, we finally arrive at the best estimate for the ^{17}O quadrupole coupling constant in H_2O (D_2O) of $6.67 \pm 0.20 \text{ MHz}$, virtually the same as the experimental value⁴² for D_2O ice ($6.66 \pm 0.10 \text{ MHz}$). Previous estimates of χ for liquid water (see for example ref 38) are higher by 15–25%, mainly due to the use of the questionable³⁹ internal field correction factor $(2\epsilon_s + \epsilon_\infty)/(3\epsilon_s)$. (It has been shown⁴³ that χ is temperature independent in the range 5–95 °C, so our conclusions from the temperature dependence of the ^{17}O relaxation rate in protein solutions are not invalidated for this reason.)

In using the χ value determined for pure water in eq 4, we have neglected any influenced from the charged protein surface on the ^{17}O quadrupole coupling constant. To examine the validity of this assumption, we performed ab initio calculations on the system $\text{Li}^+(\text{H}_2\text{O})$.⁴⁴ The components of the electric field gradient tensor at the oxygen nucleus were computed for variable oxygen–lithium distances, and different orientations. As expected, the largest effects were observed when the ion approached along a line bi-

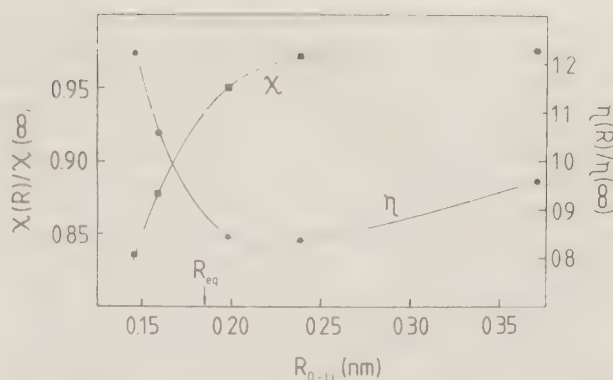


Figure 8. The water ^{17}O quadrupole coupling constant χ and asymmetry parameter η as functions of the distance to a lithium ion approaching along a line bisecting the water lone pairs. The data points were calculated as explained in ref 44.

secting the lone pairs of the water molecule (the $-x$ direction in Figure 1). The results for this case are shown in Figure 8. At the computed $\text{O}-\text{Li}^+$ equilibrium distance of 0.185 nm, χ is reduced by ca. 6%, while at a typical oxygen-charged residue distance of 0.32 nm the reduction is merely 2.5%. The asymmetry parameter passes through a minimum, and at 0.32 nm it is reduced by less than 10%. These results thus justify the approximation of an unaltered quadrupole interaction for the hydration water as compared to bulk water.

The Order Parameter. The fitted parameters $[P_{\text{PR}}(S\chi)^2]$ could now be used to obtain order parameters S with P_{PR} values calculated from the extent of hydration as determined by some other method. Now, hydration water is usually defined as the water molecules whose properties differ measurably from those of bulk water.¹ To the extent that different experimental techniques probe different interactions and are influenced differently by the dynamics in the system, this must be considered an operational definition. Thus, we will not choose this line of analysis, but rather try to estimate the order parameter, which should vary little with the nature of the protein, and then calculate the extent of hydration (from P_{PR}) for different proteins.

In a system which is anisotropic on a time scale of the order of $1/\chi$, the ^{17}O spectrum will be split into five equidistant peaks with intensity ratios²⁸ of 5:8:9:8:5 and frequency separation²⁵

$$\Delta = (3/40)P[S|\chi] \quad (8)$$

where P is the mole fraction of hydration water and the other quantities have been defined above. This equation is valid for a powder sample (no macroscopic alignment), assuming a fast exchange two-state model (hydration water and bulk water).

We chose to study the familiar water–sodium octanoate–decanol system⁴⁵ which forms lyotropic liquid crystals with surface charge densities similar to those in globular proteins. At 27 °C we obtained for the product $P[S]$ 9.40×10^{-3} for the hexagonal E phase (90.5, 9.5, 0 mol %) and 5.91×10^{-3} for the lamellar D phase (94.3, 1.5, 4.2). To get an estimate for P , we assume that

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the hydration numbers are 2–6 for the carboxylate and 1–3 for the hydroxyl groups. This yields $|S|$ values of 0.015–0.045 for the E phase and 0.026–0.077 for the D phase. Considering the similarity of the aggregate surfaces in these mesophases with the protein surface, it is reasonable to assume that the local anisotropy of the hydration water is roughly the same in both types of system. Since we are interested in the local order parameter, the value for the hexagonal phase should be multiplied by 2 (the translational diffusion around the hexagonal aggregates reduces the quadrupole interaction by a factor of 2 as compared to that of the lamellar phase²⁵). Thus, we arrive at an estimate of $|S| = 0.06 \pm 0.03$ for the hydration water of proteins.

Extent and Nature of Hydration. Using $\chi = 6.67$ MHz and $|S| = 0.06$ (cf. preceding sections) for all protein solutions together with protein concentrations (Table I) and molar masses (Table II), we calculated the extent of hydration H (grams of hydration water per 100 g of dry protein) from the fitted parameters $[P_{PR}(S\chi)^2]$. The resulting H values (Table I) correspond to approximately two molecular layers (cf. monolayer hydration in Table II) for all proteins studied except lysozyme, where the ^{17}O hydration is only slightly more than a monolayer.

When the protein concentration is increased, effects in both P_{PR} and $R_{1,PR}$ are expected. At low protein concentrations P_{PR} (and H) should increase linearly with increasing protein concentration, whereas a slower increase is expected at higher concentrations because of overlap between hydration regions. On the other hand, τ_s increases (resulting in an increased $R_{1,PR}$) with increasing protein concentration because of electrostatic repulsion between the protein molecules (see the section on dynamics of hydration). From Figure 6 it is seen that this dynamic effect dominates. The same behavior has been observed in water ^{1}H relaxation measurements on bovine serum albumin solutions.⁹

The reported magnitudes of hydration, being operationally defined and imprecise due to uncertainty in the order parameter, are of lesser interest than the variation in H with the nature of the protein. With the assumption that S varies less among different proteins than between protein and liquid crystal, the relative variations in H should be more accurate (about 20% uncertainty) than the absolute values. From Tables I and II it is seen that no correlation exists between the ^{17}O hydration and "geometrical hydration" (area/volume ratio and monolayer) or hydrodynamic hydration. Clearly, more subtle effects dominate the variation in protein hydration. A clue to the nature of these effects is provided by the pD dependence of the ^{17}O relaxation rates (Figure 7), which reveals that charged residues, particularly carboxylate, are more extensively hydrated than uncharged residues. This finding is in agreement with low-temperature proton NMR work^{1,11} on proteins and polypeptides, giving hydration numbers of 6–7.5 for anionic, 3–4.5 for cationic, 2–3 for polar uncharged, and 1 for apolar residues.

In Figure 9a the ^{17}O extent of hydration H is plotted vs. the "percentage" of charged residues (Table II) with the anionic residues weighted twice as much as the cationic ones in accord with the results of Kuntz and co-workers. The linear correlation for the "nearly neutral" (pH 5–9) protein solutions is striking, considering that individual proteins should vary in the extent of exposure of charged residues (cf. for example, the proposed "salt bridges" between subunits in HPA^{55,56}). The hydration of HPA at low pH and of cyt c at high pH deviates considerably from the general trend in Figure 9a. This is most likely due to an increased fraction of exposed uncharged polar and apolar residues at these extreme pH values (cf. the acid expansion of HPA^{55,56}), which should result in a larger intercept.

If the fast correlation time τ_f is independent of the nature of the protein, then the quantity $P_{PR}R_{1,PR}$, obtained from the fit to the dispersion data, should be proportional to H . As seen from Figure 9b, the trend is much the same: the larger scatter indicates

Table II. Physicochemical Data for Proteins

protein (source)	molar mass, ^a kg/mol	no. of subunits	exptl pH	molecular dimens, ^c nm (ref)	axial ratio ^d	R_G , ^e nm	$\tau_{\text{rot}}^{(2)f}$, ns	area/vol ratio, ^g nm ⁻¹	percent of residues ^h				estimates of hydration, g of H ₂ O/100 g of protein	
									anionic	cationic	polar neutral	apolar	mono-layer ⁱ	hydro-dynamic ^k
parvalbumin, p/ 4.25 (carp muscle)	11.50	1	8.99	3.0 × 3.0 × 3.6 (46)	1.2	1.2	2.9	1.9	19.1	12.3	24.1	44.5	41.9	
cytochrome c, ferri (horse heart)	12.38	1	5.22 10.49	2.5 × 2.5 × 3.7 (47)	1.5	1.1	2.4	2.2	10.8	22.8	35.8	30.5	31.2	24
lysozyme (hen egg white)	14.32	1	5.11	3.0 × 3.0 × 4.5 (48)	1.5	1.4	4.2	1.8	7.6	14.5	43.6	34.4	39.9	57
hemoglobin, oxy (human)	64.37	4	9.17	5.0 × 5.5 × 6.4 (49)	1.2	2.2	13	1.1	11.5	9.2	31.9	47.4	23.6	74 ^l
plasma albumin (human)	66.50	3 ^b	5.09 2.18	3.5 × 3.5 × 14.0 (50)	4.0	3.3	40	1.4	15.6	17.0	27.4	50.2	28.0	35
alcohol dehydrogenase, apo (horse liver)	79.87	2	5.73	4.5 × 6.0 × 11.0 (51)	2.1	3.0	31	1.0	0.3	17.1	42.7	39.9	28.9	37
immunoglobulin G, polyclonal (human)	150.0	3 ^b	6.0						5.5	11.3	46.3	36.9		

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^a From amino acid composition. ^b Covalently linked. ^c From X-ray crystallography, i.e., excluding hydration water. ^d For prolate ellipsoid: $2a \times 2a \times 2c$, $n = c/a$. ^e Radius of gyration for prolate, $R_G = c[(2/n^2 + 1)/5]^{1/2}$. ^f For a sphere of radius $R = R_G + 0.3$ nm, obeying the Debye-Stokes-Einstein relation $\tau_{\text{rot}}^{(2)} = 4\pi\eta R^3/(3kT)$, where $T = 300$ K and $\eta = 8.50 \times 10^{-4}$ kg ms⁻¹. ^g For prolate: $A/V = (3/2c)[1 + (n/x)] \arcsin x$, where $x = (1 - 1/n^2)^{1/2}$. ^h At experimental pH, assuming all residues available for titration with pK values from ref 36 or ref 33 (HPA). ⁱ For prolate and 0.12 nm² surface area per H₂O molecule. ^j From sedimentation and diffusion coefficients.⁵² ^k Horse hemoglobin.

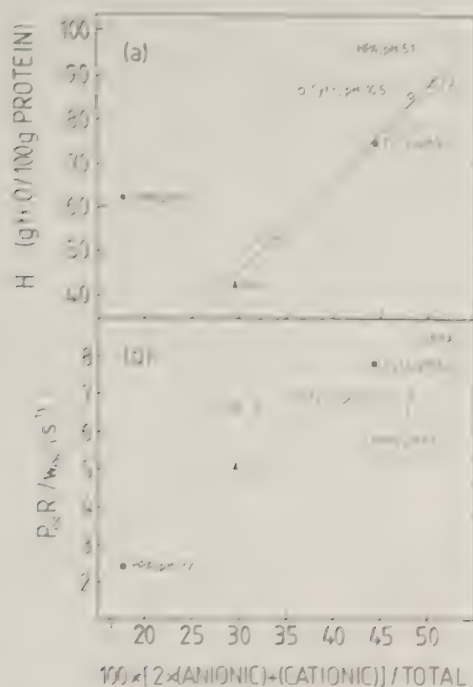


Figure 9. (a) The extent of hydration (from ^{17}O relaxation) vs. "percentage" (weighted) of charged residues. The line is a least-squares fit to the five data points in the pH range 5–9 (see Table I). (b) The normalized fast contribution to the ^{17}O excess relaxation rate vs. "percentage" (weighted) of charged residues.

a small variation in τ_f with the nature of the protein (cf. next section). Note that the correlation evident from Figure 9b is independent of any assumptions about the order parameter (as long as $S^2 \ll 1$).

The water-HPA interaction in the acidic pH range deserves special consideration. From Figures 7a and 9 it is clear that an appreciable reduction in hydration occurs as pH (pD) is lowered from 5 to 2. The decrease in excess ^{17}O relaxation rates in Figure 7a is, however, partly due to a variation in the slow correlation time τ_s . This follows from the much larger effect on $R_{2,ex}$ as compared to $R_{1,ex}$ and accordingly the fitted τ_s decreases from 16 ns at pH 5.1 to 9 ns at pH 2.2 (Table I). (A reduced correlation time for the expanded HPA molecule was also deduced from ^{35}Cl magnetic relaxation studies³³ and is explained by independent reorientation of the subunits.) The decrease in H between pH 5.1 and 2.2 is 27% (Figure 9a), in good agreement with the low-temperature proton NMR results¹¹ of 24%. Other measurements have, however, been interpreted as an increased hydration upon lowering of pH from 5 to 2, by 67% according to measurements of the H_2^{18}O self-diffusion coefficient⁵⁷ and by 50% according to dielectric relaxation studies.⁵⁸ Without going into a detailed discussion of the theoretical basis of the data reduction in these techniques, we want to point out the possibility that these results are influenced by the greatly increased size and anisotropy of the albumin molecule which occurs during the N-F transition around pH 4.2 and the acid expansion in the pH range 2–4.^{55,56}

Dynamics of Hydration. The fast correlation time τ_f for the local, slightly anisotropic water reorientation was calculated from the ratio of the two composite parameters by using an order parameter $[S] = 0.06$ (cf. above). As expected τ_f is, within the estimated uncertainty (ca. 30% not counting the uncertainty in S , otherwise of the order 100%), the same for all protein solutions (except possibly HPA at pH 2.2) with an average of 20 ps (Table I). Thus the hydration water is, on the average, hindered in its reorientational motion by a factor of ca. 8 relative to bulk water ($\tau_{rot}^{(2)} = 2.40$ ps for pure H_2O at 27.0 °C according to the di-

electric data cited above). This is of the same order of magnitude as the slowing down of the hydration water reorientation in aqueous electrolyte solutions found by NMR relaxation⁶⁰ (e.g., a factor of 1.5–3.5 for CO_3^{2-} , CCl_3COO^- , Li^+ , and Na^+). On the other hand, a large amount of dielectric^{1,74} and magnetic^{9,75} relaxation data from aqueous protein solutions have been interpreted in terms of hydration water correlation times in the nanosecond (or even microsecond⁷²) range. Such slow reorientational rates are clearly inconsistent with our data.

The shorter τ_f of 9 ps found for HPA at pH 2.2 (Table I) is explained by the fact that virtually all the ca. 105 carboxylate groups, which otherwise make a major contribution to the slowing down of water reorientation, are protonated at this pH.

The slow correlation time τ_s (Table I), obtained directly from the fit to the dispersion data, is in all cases (except for HPA) significantly longer than the rotational correlation time $\tau_{rot}^{(2)}$ calculated from the Debye-Stokes-Einstein equation with the radius of gyration corrected for hydration (Tables I and II). Similarly long correlation times have been observed by other methods, e.g., proton and deuteron NMR dispersion,^{4,6} ^{13}C relaxation,⁶¹ light scattering,⁶² and dielectric relaxation.^{63,64} As an explanation we suggest that electrostatic repulsion between the densely spaced (cf. mean center-to-center distance in Table I) and highly charged protein molecules has an ordering effect on the system. This hypothesis is supported by the fact that concentrated solutions of micelles⁶⁵ and polyelectrolytes⁵³ yield X-ray diffraction patterns and thus are lattice-like. If this long-range Coulombic protein-protein interaction is important, one would expect a decreased τ_s with increasing salt concentration. This is indeed found; only for HPA was the ^{17}O dispersion measured in the presence of added electrolyte (0.15 M KCl) and here τ_s is smaller than the calculated $\tau_{rot}^{(2)}$. The hypothesis also predicts that τ_s should increase with increasing protein concentration; that this is the case can be seen from the HPA data in Table I (note that τ_s for the intermediate concentration refers to a slightly lower temperature) and from the protein concentration dependence for Lyz and HPA (see above). The variation in the ratio $\tau_s/\tau_{rot}^{(2)}$ (Table I) is probably due to structural differences; the ordering effect should increase with increasing molecular anisotropy.

Concluding Discussion

We now recapitulate the arguments that led us to formulate the model defined by eq 3 and 4 and then summarize the main results from our ^{17}O relaxation data analyzed in terms of this model. First it is quite clear (cf. Figures 3–5) that the dispersion of the excess relaxation rates cannot be described by a single correlation time, i.e., by a simple two-state fast exchange model, rather a two-correlation time model is needed. Now, the two correlation times for the hydration water may be interpreted in two ways.

The first model, which, with various modifications, has been used in most protein hydration NMR dispersion work (see, for example, ref 4, 6–10), consists of two physically distinct classes of hydration water. Such a model is unsatisfactory for two reasons. (i) It is unlikely that two classes of hydration water, both in the fast exchange limit, should have reorientation times differing by 3 orders of magnitude. (ii) If the long correlation time is associated with rigidly bound water molecules, then unreasonably low degrees of hydration result; putting $S = 1$ in eq 4b reduces all H values by a factor of 3.6×10^{-3} ; e.g., for lysozyme this leads to the absurd situation that the enhancement of the relaxation rate is due

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to 1.2 water molecules (cf. ref 4 and 6).

In the other type of two-correlation time model there is only one class of hydration water, i.e., this is a two-state model. Due to the influence of the protein surface, the reorientation of the hydration water is anisotropic; hence it must be described by two correlation times. This model is consistent with the magnitude of the two correlation times τ_f and τ_s and is also physically attractive in view of the similarity of the local environment near a protein surface and that in anisotropic lyotropic liquid crystals. Similar models have been used to interpret nuclear magnetic relaxation data in solutions of micelles²⁵ and biological macromolecules.^{66,73} Recently a qualitative reinterpretation of previous^{4,6} proton and deuterium dispersion data for protein solutions using this model has been published.⁶⁷ In that work, however, the contribution from the fast motion (eq 4a) was neglected.

The emerging picture of protein hydration is intermediate between the two extremes of polarized multilayers⁶⁸ on the one

hand and a small number of irrotationally bound water molecules^{4,6} on the other. Approximately two layers of water are, on the average, hindered in their reorientation by a factor of ca. 8. This rapid local motion has a small anisotropic component which is averaged out by protein reorientation. Charged residues, particularly carboxylate, are more extensively hydrated than other residues. This fact accounts for the variation in the extent of hydration between different proteins (Figure 9a).

Note Added in Proof: Since the completion of this work, it has been shown⁷⁹ that existing analytical expressions⁸⁰ for the relaxation rates, i.e., for the functions $f_i(\tau_s, \omega_0)$ in eq 4b, are accurate to better than 2% for the present data. The numerical diagonalizations of the relaxation matrices that were performed in this work, although correct, are thus unnecessary. Furthermore, a detailed derivation and discussion of the "two-step averaging" relaxation model (eq 3–5) will appear shortly (Wennerström, H.; Halle, B. *J. Chem. Phys.*, submitted).

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VI

PROTOTROPIC CHARGE TRANSPORT IN WATER

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The mechanism of prototropic charge transport in liquid water is investigated in the light of recent advances in the structural characterization of water and hydrated prototropic ions. We report new oxygen-17 scalar relaxation data for normal and heavy water as well as KCl solutions. The conventional theory for deriving proton jump frequencies from NMR data is revised and extended. Our NMR results are combined with conductivity data to gain insight about the mechanism. Three limiting models for prototropic charge transport are formulated and tested against experiment. We argue that the current view of proton transfer in water should be revised in several respects. Our analysis indicates that short concerted transfer processes take place. Water reorientation does not appear to be involved in the rate-limiting step. The charge is thought to migrate preferentially to prehydrated sites (energetic sinks) in the water structure. As a consequence, also the Stokesian contribution to prototropic charge transport is anomalously fast.

1. INTRODUCTION

The mechanism of prototropic charge transport in liquid water is a problem which dates back to the early days of physical chemistry as a distinct scientific discipline. The first major step towards an understanding of the anomalously high apparent mobilities of the prototropic species H_3O^+ and OH^- was taken in 1905 by Danneel¹, who recognized that intermolecular proton transfer can lead to charge transport at a rate exceeding that of mass transport. Hückel², in 1928, used this basic idea to develop the first formal theory of prototropic charge transport. Five years later an improved treatment, incorporating quantum-mechanical considerations, was presented in the classic paper by Bernal and Fowler³. In 1949 Gierer and Wirtz⁴ performed a detailed analysis of the problem and extended the theory by explicitly introducing effects of water structure. Much of the theoretical debate has been concerned with the nature of the rate-limiting step in prototropic charge transport. Thus Conway, Bockris and Linton⁵ as well as Eigen and De Maeyer⁶, in two influential papers published in the late fifties, favoured water reorientation as the rate-limiting step. This, of course, does not exhaust the list of contributions bearing on the problem of prototropic charge transport - the literature on the subject is prodigious. Some of the most extensive and penetrating reviews are those by Gierer and Wirtz⁴, Conway⁵, Eigen and De Maeyer⁶, and - more recently - by Stillinger⁷.

Despite this continuous effort over a period of 75 years, there exists today no "ab initio" theory which can quantitatively account for all the anomalous facets of prototropic charge transport: the high mobility, the dependence on temperature and pressure, the effect of added salt and isotope substitution, the difference between positive and negative charge transport, etc. Considering our limited knowledge about the structure and dynamics of water and of vibrational relaxation in liquids, this state of affairs is hardly surprising. Although a detailed quantum-statistical theory seems out of reach at present, we nevertheless believe that the time is ripe for a re-examination of certain aspects of the prevailing semi-empirical theories of prototropic charge transport.

Guided by recent advances⁸ in the understanding of water structure - mainly from computer simulation studies - and by the detailed characterization of hydrated prototropic ions provided by ab initio quantum-mechanical calculations⁹⁻¹⁴, we shall formulate and discuss three limiting models of prototropic charge transport: fluctuation transfer, Markovian transfer, and concerted transfer. Special emphasis will be laid on concerted transfer, for which we develop a topological model. This allows us - in a semi-empirical way - to calculate the length distribution of proton transfer chains taking into account H-bond polarity correlation and various modes of chain termination.

In testing these models against experiment, our approach will be to combine nuclear magnetic resonance (NMR) data on rate constants with electric conductivity data. The application of the NMR technique to prototropic charge transport was pioneered by Meiboom¹⁵ 20 years ago. Here we report new data - obtained from oxygen-17 NMR - on the prototropic rate constants in normal and heavy water as well as in KCl solutions. We derive an equation for ¹⁷O scalar relaxation in D₂O and discuss - in connection with new data - the problem of obtaining an accurate value for the ¹⁷O-¹H spin-spin coupling constant. Furthermore, we point out inconsistencies in previous treatments relating rate constants to lifetimes. In this connection we consider the effect, on the measured rate constants, of the time-dependent probability for the re-encounter of a given water molecule with a given prototropic charge.

By combining NMR and conductivity data it is possible to distinguish between Markovian and concerted proton transfer. Further insight about the mechanism of prototropic charge transport is provided by the experimental data on the effect of temperature, pressure, salt, and isotope substitution. Our analysis indicates that concerted proton transfer does occur, but only over two or three H-bonds. We argue that water reorientation cannot be involved in the mechanism - a more likely candidate for the rate-limiting step would be a collective stretching and bending of H-bonds, as recently suggested by Newton¹⁰. We believe that the prototropic charge

migrates preferentially to "prehydrated" sites - energetic sinks with pre-existing H-bonds of the appropriate polarity. On account of their extremely short lifetimes, prototropic ions exhibit no long-range hydration effects. Consequently, also the "normal" (Stokesian) contribution to prototropic mobilities may be anomalously high. This conclusion receives support from our analysis of the experimental data.

We are not presenting a comprehensive theory of prototropic charge transport here. In fact, we probably raise more questions than we answer. However, in dealing with a problem of this degree of complexity, it is important to explore in some detail the component parts that ultimately may combine into a general theory. In addition, we hope that some of the concepts introduced here will prove useful in connection with computer simulation studies - a promising approach to this problem which has recently been initiated by Stillinger and coworkers^{7,16,17}.

2. OXYGEN-17 NMR

2.1 RELAXATION THEORY

The spin relaxation of oxygen-17 nuclei in liquid water can proceed via two different mechanisms. Quadrupolar relaxation is due to the modulation, through molecular reorientation, of the interaction between the ^{17}O nuclear electric quadrupole moment and electric field gradients at the nucleus. The quadrupolar contribution R_Q to the relaxation rate is given by¹⁸

$$R_Q = \frac{12\pi^2}{125} \chi^2 (1 + \eta^2/3) \tau_{\text{rot}} \approx 5.43 \cdot 10^{13} \tau_{\text{rot}}, \quad (1)$$

where values¹⁹ for the water ^{17}O quadrupole coupling parameters have been inserted[†]. At 300 K, the rotational correlation time^{19,20} τ_{rot} is 2.4 ps (3.1 ps in D_2O), corresponding to $R_Q \approx 130 \text{ s}^{-1}$ (168 s^{-1}).

The second contribution to the water ^{17}O relaxation rate originates in the finite lifetime of the chemical bonds in the water molecule. The scalar, electron-mediated, interaction between the ^{17}O and the ^1H (or ^2H) nuclear magnetic moments is thus modulated by the exchange of either of the two water protons (or deuterons). This so-called scalar relaxation of the first kind contributes significantly only to the transverse relaxation rate. For sufficiently fast exchange (see below) one finds¹⁸

$$R_S(\text{H}_2\text{O}) = 4\pi^2 J_{\text{OH}}^2 \tau_{\text{exc}} \approx 2.60 \cdot 10^5 \tau_{\text{exc}}, \quad (2a)$$

$$R_S(\text{D}_2\text{O}) = \frac{32\pi^2}{3} J_{\text{OD}}^2 \tau_{\text{exc}} \approx 1.63 \cdot 10^4 \tau_{\text{exc}}, \quad (2b)$$

[†] The quadrupole coupling is virtually independent of temperature and H/D isotope substitution.

where values for the spin-spin coupling constants (sect. 2.2) have been inserted. On comparing eqn (1) and (2) we see that the spin-spin coupling is weaker than the quadrupole coupling by 8 or 9 orders of magnitude. In neutral water, however, the exchange time τ_{exc} is longer than the rotational correlation time τ_{rot} by roughly the same factor, making the contributions R_Q and R_S to the transverse relaxation rate of similar magnitude.

For exchange times of the same order of magnitude as the inverse spin-spin coupling $(2\pi J)^{-1}$, the conventional perturbation theory of spin relaxation breaks down¹⁸. Since this happens for H_2O , and even more so for D_2O , in the neutral pH range, it becomes necessary to derive more accurate expressions for R_S .

To first order in the spin-spin coupling[†], the time-independent spin Hamiltonian for the ^{17}O spin in the water molecule can be written¹⁸

$$\hat{H}_O/\hbar = \omega_O \hat{I}_{ZA} + 2\pi J \hat{I}_{ZA}(\hat{I}_{ZB} + \hat{I}_{ZC}), \quad (3)$$

where the subscript A refers to the ^{17}O spin and B and C to the two proton (deuteron) spins. The corresponding eigenvalues are

$$E_{mM}/\hbar = m\omega_O + mM 2\pi J, \quad (4)$$

where m and M are the eigenvalues of $\hat{I}_{ZA}$ and of $(\hat{I}_{ZB} + \hat{I}_{ZC})$, respectively. Consequently, we find for the angular frequencies of the ^{17}O transitions $\Delta m = 1$, $\Delta M = 0$

$$\omega_{OM} = \omega_O + M 2\pi J. \quad (5)$$

[†]The first order treatment is valid provided that $2\pi J \ll \omega_O(^1\text{H}, ^2\text{H}) - \omega_O(^{17}\text{O})$. This condition is easily satisfied for the magnetic fields of interest here.

If the rate of transitions among states with different M-values is slow compared to the spin-spin coupling, the ^{17}O absorption consists of a triplet ($M = 0, \pm 1$) in H_2O and a quintet ($M = 0, \pm 1, \pm 2$) in D_2O . The relative intensities of the multiplet components are given by the degeneracies of the energy eigenstates as 1:2:1 and 1:2:3:2:1, respectively. As the M-transition rate increases through proton (deuteron) exchange[†], the individual lines first broaden whereafter the multiplet structure collapses into a single line, which approaches Lorentzian shape and becomes progressively narrow.

The effect of proton (deuteron) exchange on the ^{17}O lineshape may be described in terms of the generalized Bloch equations^{15,21}, which under steady-state, nonsaturation conditions take the form

$$[R_Q + \frac{1}{\tau_{\text{exc}}} + i(\omega - \omega_{\text{OM}})]G_M - \frac{1}{\tau_{\text{exc}}} \sum_{M'} A_{M-M'} G_{M'} = i\omega_1 M_{\text{eq}} P_M. \quad (6)$$

Here G_M is the complex transverse magnetization, in the rotating frame, for the M:th state with relative population P_M . M_{eq} is the equilibrium magnetization, ω is the observed (angular) frequency, and ω_1 is the product of the ^{17}O magnetogyric ratio γ and the radiofrequency field B_1 . The coefficients $A_{M-M'}$ follow from the relative populations and the principle of detailed balancing. In matrix form

$$A(\text{H}_2\text{O}) = \frac{1}{4} \begin{bmatrix} 2 & 2 & 0 \\ 1 & 2 & 1 \\ 0 & 2 & 2 \end{bmatrix}, \quad (7a)$$

[†] M-transitions can, of course, be induced also by proton (deuteron) relaxation. However, in the pH range of interest, the exchange rates exceed these relaxation rates by at least two orders of magnitude.

$$\underline{A} (D_2O) = \frac{1}{18} \begin{bmatrix} 6 & 6 & 6 & 0 & 0 \\ 3 & 6 & 6 & 3 & 0 \\ 2 & 4 & 6 & 4 & 2 \\ 0 & 3 & 6 & 6 & 3 \\ 0 & 0 & 6 & 6 & 6 \end{bmatrix} . \quad (7b)$$

The system of equations (6) is valid provided that (1) the duration of the exchange event is short compared to τ_{exc} , (2) $1/\tau_{exc}$, $2\pi J \ll \omega_0(^1H, ^2H) - \omega_0(^{17}O)$, and (3) $\tau_{exc} \gg \tau_{rot}$. These conditions are all satisfied in the present case.

After substitution of (5) and (7), it is straightforward to solve the linear system (6) for the total complex magnetization $G = \sum_M G_M$. The result is

$$\frac{G(H_2O)}{i\omega_1 M_{eq} \tau_{exc}} = \frac{2(2S^2 + S + K^2)}{4S^3 - (1 - 4K^2)S} , \quad (8a)$$

$$\frac{G(D_2O)}{i\omega_1 M_{eq} \tau_{exc}} = \frac{108S^4 + 72S^3 + (9 + 396K^2)S^2 - (2 - 144K^2)S + (4 + 144K^2)K^2 - 1/3}{108S^5 - (39 - 540K^2)S^3 - 8S^2 + (1 - 60K^2 + 432K^4)S + 2/9} . \quad (8b)$$

Here we have introduced the dimensionless parameters

$$K \equiv 2\pi J \tau_{exc} , \quad (9)$$

$$S(H_2O) \equiv R_Q \tau_{exc} + \frac{1}{2} + i(\omega - \omega_0) \tau_{exc} , \quad (10a)$$

$$S(D_2O) \equiv R_Q \tau_{exc} + 2/3 + i(\omega - \omega_0) \tau_{exc} . \quad (10b)$$

Under the conditions of the present study, τ_{exc} is sufficiently short for the multiplet structure to collapse into an essentially Lorentzian absorption line. Very little information is then lost if

we characterize the lineshape by a single (apparent) relaxation rate R_S , related to the full width at half amplitude through $R_S = \frac{1}{2} \Delta\omega_{\frac{1}{2}}$. The theoretical linewidth $\Delta\omega_{\frac{1}{2}}$ is obtained numerically from the absorption lineshape as given by the imaginary part of G in eqn (8).

With the "exact" solution (8) at hand, it is now possible to assess quantitatively the accuracy of eqn (2). For given values of τ_{exc} , R_Q , and J we have computed the exact R_S by means of eqn (8). This value for R_S was then inserted into eqn (2) to yield an approximate exchange time τ'_{exc} . In fig. 1 we have plotted the ratio τ_{exc}/τ'_{exc} versus $\log \tau_{exc}$ and the corresponding exact R_S . In these calculations we have used $R_Q = 130 \text{ s}^{-1}$, $J_{OH} = 81.1 \text{ Hz}$ for H_2O and $R_Q = 168 \text{ s}^{-1}$, $J_{OD} = 12.45 \text{ Hz}$ for D_2O . For exchange times shorter than ca. 1 ms, the expressions (2) are reasonably accurate, whereas for slower exchange the accuracy deteriorates rapidly, more so for H_2O than for D_2O . While eqn (2a) may be of quantitative value in certain cases, eqn (2b) actually fails badly under the conditions of interest here. This happens because the exchange is slower in D_2O than in H_2O (sect. 2.3). In the present work, we have used eqn (8) in analysing the ^{17}O relaxation data from D_2O as well as from H_2O . However, because of its simplicity, eqn (2) will prove useful for qualitative considerations.

2.2 THE SPIN-SPIN COUPLING

To obtain the exchange time τ_{exc} from the measured apparent relaxation rate R_S , we must know the value of the spin-spin coupling constant J . Since this quantity is bilinear in the magnetic moments involved¹⁸, so that $J_{OH}/J_{OD} = \gamma_H/\gamma_D = 6.514$, only one of the two constants has to be determined. In the domain of validity of eqn (2), $1/\tau_{exc}$ is clearly proportional to J^2 . Using eqn (8) we actually find that, in the experimentally interesting range, $1/\tau_{exc}$ is even more sensitive to J - for D_2O the dependence is stronger than the third power[†]. To obtain kinetic parameters of high

[†] Some authors^{22,23} have erroneously concluded that $1/\tau_{exc}$ is proportional to J .

accuracy, it is thus crucial to have a reliable estimate of J .

The ^1H - ^{17}O spin-spin coupling constant in H_2O can, in principle, be determined experimentally in several ways. The most obvious strategy is to observe directly the multiplet structure under conditions of sufficiently slow exchange, e.g. in water diluted in organic solvents or in the vapour phase. One can then observe either the proton sextet or the ^{17}O triplet. However, the proton multiplet is found to be less well resolved than the ^{17}O multiplet. This observation can be rationalized by a consideration of transition probabilities^{18,24}, which shows that the lifetimes of the six individual ^{17}O states ($m = \pm 1/2, \pm 3/2, \pm 5/2$) are shorter than the ^{17}O relaxation time by factors $8/18$ ($m = \pm 1/2$), $8/23$ ($m = \pm 3/2$), and $8/15$ ($m = \pm 5/2$). Furthermore, the central part of the ^1H sextet is hidden by the uncoupled signal from protons bound to ^{16}O or ^{18}O .

A second approach to determine J consists in measuring the scalar relaxation rate R_S as a function of the pH of an aqueous solution. However, to the extent that eqn (2) is valid, this approach is not feasible. The reason is that τ_{exc} is proportional to a function of pH (sect. 2.3) and one can thus determine only the product of J^2 and this (unknown) proportionality constant. Since eqn (2a) is accurate to within a few percent (fig. 1), we cannot expect to determine J_{OH} with any accuracy from the ^{17}O scalar relaxation in H_2O . Measurements on D_2O , on the other hand, should be more informative about J , since the exchange is slower in D_2O (sect. 2.3), thereby producing a non-linear J^2 -dependence [cf. eqn (8)]. A precise determination of J by this method, however, requires data of higher accuracy than ours (fig. 4 and 5), which yield $J_{\text{OH}} = 78 \pm 4$ Hz. Although this result is not very precise, it should be noted that our D_2O data could not be fitted, within the experimental uncertainty, with the commonly adopted value of 92 Hz (see below).

The situation for proton scalar relaxation is further complicated by the short ^{17}O quadrupolar relaxation time (7.7 ms at 300 K), which contributes to the ^1H linewidth through so-called scalar relaxation of

the second kind¹⁸. To correct for this effect, various approximate formulas^{15,25} have been suggested, but too short ^{17}O T_1 values have been used with the result that the corrected J_{OH} values have come out too large. Employing this method, Meiboom¹⁵ found $J_{\text{OH}} = 92 \pm 15 \text{ Hz}$ - a value which has been adopted in most subsequent NMR studies^{22,26-28} of proton transfer in water.

J_{OH} has been determined also from ^1H relaxation in the rotating frame by Burnett and Zeltmann²⁹, who found $J_{\text{OH}} = 89.8 \pm 2.3 \text{ Hz}$. Furthermore, pulse techniques have been used by several workers^{30,31} with results close to 97 Hz. Recently, proton exchange in H_2O has been studied also through the low-frequency proton T_1 dispersion³². J_{OH} values in the range 86 - 98 Hz were found.

We believe that the most reliable determinations of J_{OH} are those based on the direct observation of the ^{17}O triplet under slow exchange conditions. In table 1 we have compiled the available results, including a few of our own, obtained by this method. All of the results from resolved triplets are in close agreement, with a mean of $81.0 \pm 1.4 \text{ Hz}^{\dagger}$. Considering the variation in temperature, concentration, and solvent hydrogen bonding capability, variables which strongly affect for example the chemical shift^{36,38}, it appears that the spin-spin coupling is insensitive to intermolecular perturbations. This conclusion is further corroborated by the observed²⁹, temperature independence (4- 46°C) of J_{OH} in pure water and by the similarity with the J_{OH} values 85.5 and 83.6 Hz determined³⁹ for the hydroxyl bond in methanol and ethanol, respectively. (As in the case of water, no significant temperature or concentration dependence in J_{OH} was observed for the alcohols^{34,39}). In summary, we believe that there are compelling reasons for taking $J_{\text{OH}} = 81 \text{ Hz}$ as the best estimate for pure liquid water.

Another way to investigate the effect on J_{OH} of intermolecular perturbations is by means of quantum-mechanical calculations. Although considerable

[†] The sign of J_{OH} is actually negative, but since scalar relaxation depends on J^2 [cf. eqn (2) and (8)] we have omitted the sign throughout this paper.

progress has been made⁴⁰ in recent years in obtaining reliable computational results for J_{OH} in the water molecule, a strong basis set dependence, large correlation effects, and important contributions from non-contact terms combine to limit the accuracy of reported results to something like $\pm 10\%$. Moreover, all calculations reported to date refer to the monomer with gas-phase geometry. However, recent coupled Hartree-Fock calculations (A. Laaksonen, unpublished results) at variable molecular geometry show that the dominating Fermi contact term varies rather slowly (approximately as r^{-3}) with the internuclear separation. Since the O-H bond length varies less than 1 pm between monomer and bulk liquid water^{41,42}, the effect of a possible bond length perturbation is not likely to exceed 2.5 Hz. To obtain accurate data for the effect of hydrogen bonding on J_{OH} would require extensive calculations, which probably have to await further methodological progress.

2.3 THE RATE CONSTANTS

The exchange time τ_{exc} , introduced in sect. 2.1, is defined more precisely as the mean time between events whereby one of the water protons (deuterons) is exchanged for a different one. These events will in the following be referred to simply as exchanges, with the understanding that there may occur also "NMR-inactive" exchanges whereby the same proton (deuteron) is transferred to and from (or vice versa) a given water molecule. This and other matters relating to the detailed exchange mechanism will be deferred to the following sections. As for now, we require only that the duration of the exchange event be short compared to τ_{exc} - an assumption underlying eqn (6).

Consider a system containing N_w water molecules, N_+ positive, and N_- negative prototropic charges. By using the term prototropic charge, rather than hydronium or hydroxide ion, we imply that the instantaneous atomic configuration of the charged species can be

left unspecified at this stage. After addition of acid or base (making $N_+ \neq N_-$) or of salt there are of course other charged species in the system. These species are assumed to be incapable of effecting exchanges and their presence will not show up explicitly in the formalism. They may, however, affect the mechanism of exchange induced by prototropic charges and also the numbers $N_{\pm}$.

Let R denote the mean number of exchanges occurring in the entire system in unit time (the mean total exchange rate) and let $r_{\pm}$ be the mean number of exchanges effected by a given prototropic charge (of indicated sign) in unit time and at infinite dilution with respect to prototropic charges (the limiting mean specific exchange rate). Since $N_{\pm}/N_w \lesssim 10^{-7}$ in the experimentally interesting pH range, we may safely neglect the effect of prototropic charge-charge interaction on the exchange rate[†]. Thus

$$R = r_+ N_+ + r_- N_- \quad (11)$$

By definition, $1/\tau_{\text{exc}}$ is the mean number of exchanges experienced by a water molecule in unit time. Hence

$$R = \frac{N_w}{\tau_{\text{exc}}} \quad (12)$$

Introducing molarities through

$$\frac{c_{\pm}}{c_w} = \frac{N_{\pm}}{N_w} \quad , \quad (13)$$

[†] According to the Debye-Hückel-Onsager limiting law, the molar conductivity Λ varies with concentration as $\Lambda = \Lambda_0 - (60.2 + 0.229 \Lambda_0) c^{\frac{1}{2}}$ at 25°C. With $\Lambda_0(\text{HCl}) = 426 \text{ S cm}^2 \text{ mol}^{-1}$ we find for $N_+/N_w = 10^{-7}$ that $1 - \Lambda/\Lambda_0 = 8.7 \cdot 10^{-4}$, which is negligible.

we find

$$\frac{1}{\tau_{\text{exc}}} = k_+ c_+ + k_- c_- , \quad (14)$$

where we have defined the second-order rate constants

$$k_{\pm} \equiv \frac{r_{\pm}}{c_w} . \quad (15)$$

It remains for us to relate the molarities $c_{\pm}$ to the measured pH values. If the difference in liquid junction potential between the standard buffers and the sample solution may be neglected[†], we have⁴³

$$\text{pH} = - \log a_+^m = - \log \gamma_+^m m_+ , \quad (16)$$

where a_+^m denotes the H_3O^+ activity (molarity scale), γ_+^m the corresponding activity coefficient, and m_+ the molality. A similar relation holds for pD, which is obtained from the instrument reading pH_D from a D_2O solution, with the glass electrode calibrated in standard H_2O buffers, through⁴⁴

$$\text{pD} = \text{pH}_D + (0.45 \pm 0.03) . \quad (17)$$

With m_+ obtained via eqn (16) and (17), m_- is determined by the ion product Q_w^m according to

$$\frac{K_w^m}{F_w^m} = Q_w^m = m_+ m_- , \quad (18)$$

[†] The validity of this assumption was verified by showing that the "operational" activity coefficient, obtained from eqn (16) with known pH and m_+ , agrees to within 2 % with γ_+ obtained from independent electrochemical data (assuming $\gamma_+ = \gamma_-$) or from the Debye-Hückel theory.

where $K_W^m \equiv a_+^m a_-^m / a_W^x$ is the thermodynamic dissociation constant for water and where $F_W^m = \gamma_+^m \gamma_-^m / a_W^x$ is the activity coefficient function. Finally, the molalities $m_{\pm}$ are converted to molarities $c_{\pm}$ using solution densities and salt concentrations. The relation between molarities and pH (or pH_D) may then be written[†]

$$c_{\pm} \alpha_{\pm} = 10^{\mp pH} . \quad (19)$$

The conversion factors $\alpha_{\pm}$ for the four solutions studied are given in table 2.

TABLE 2

According to eqn (8), the apparent scalar relaxation rate R_S is a function of (1) the quadrupolar relaxation rate R_Q , (2) the spin-spin coupling constant J , and (3) the exchange time τ_{exc} . Since, under the experimental conditions, the functional dependence on τ_{exc} is monotonic, the condition for a maximum in R_S versus pH (or pH_D) is $\partial(1/\tau_{exc})/\partial pH = 0$. From eqn (14) and (19) we then find the following relations for the quantities pH^* (or pH_D^*) and τ_{exc}^* referring to the extremum

$$pH^* = \frac{1}{2} \log \left(\frac{\alpha_- k_+}{\alpha_+ k_-} \right) , \quad (20)$$

$$\tau_{exc}^* = \frac{1}{2} \left(\frac{\alpha_+ \alpha_-}{k_+ k_-} \right)^{\frac{1}{2}} . \quad (21)$$

There are two points worth noting about these relations. First, according to eqn (20), the ratio k_+/k_- is fully determined by the position pH^* of the maximum in R_S and by the conversion factors $\alpha_{\pm}$. In particular,

[†] Eqn (19) implies that the conversion factors $\alpha_{\pm}$ are independent of pH. This is not strictly true, but since all data points in the range $5 \lesssim pH \lesssim 9$ were measured before any points at extreme pH values, the effect of varying ionic strength can be neglected even in the absence of added salt.

k_+/k_- is independent of J. Second, if the isotope effect were confined to J one would expect the maximum exchange broadening in D_2O to be merely 6 % of that in H_2O (fig. 1, upper scale). Since the experimental figure is three times larger (fig. 2-5), the exchange must be slower in D_2O than in H_2O . According to eqn (21) this is due to the lower (by a factor 1/9) ion product in D_2O and also to a kinetic isotope effect on the rate constants $k_{\pm}$ (see below).

G. 2-5

The experimental data from the four solutions studied are displayed in fig. 2 - 5. The curves are results of direct least-squares fits by the Marquardt algorithm⁵⁰ of the two parameters k_+/α_+ and k_-/α_- in the theoretical R_S - pH relation defined by eqn (8), (14), and (19). The spin-spin coupling constants were fixed at $J_{OH} = 81.1$ Hz and $J_{OD} = 12.45$ Hz (sect. 2.2) and R_Q was taken from the linewidth at extreme pH values[†]. To allow for experimental uncertainty in pH as well as in R_S , we minimized the sum of the squares of the perpendicular - rather than the vertical - distances from the curve. (If the error in pH were neglected, undue weight would be given to the data points on the steep portions of the curves.)

BLE 3

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The rate constants resulting from the fits to the data in fig. 2-5 after substitution of the conversion factors (table 2) are recorded in table 3 together with experimental details. While the fits to the H_2O data are excellent, one can discern a systematic deviation in the "wings" of both D_2O curves. The origin of this deviation will be discussed in sect. 4.1. In table 4 we compare our rate constants for pure H_2O with previous

[†] Introduction of a third parameter to account for the small (and constant) contribution to the linewidth from magnetic field inhomogeneity did not improve the fits. This is not unexpected since R_S depends on R_Q only to second order. [Compare eqn (2), in which R_Q does not appear.]

results corrected to 28.0°C and $J_{OH} = 81.1$ Hz (see footnote to table 4). Our k_+ value is larger than all previous determinations, whereas our k_- value agrees with most of the earlier results.

We believe that the following experimental results, taken from table 3, can serve to test models for the mechanism of prototropic charge transfer in water (all data at 28°C):

- (1) $k_+ = 7.1 \cdot 10^9 \text{ M}^{-1}\text{s}^{-1}$ and $k_- = 3.4 \cdot 10^9 \text{ M}^{-1}\text{s}^{-1}$ in H_2O ,
- (2) the "acidic" mechanism is more efficient than the "basic" one by a factor of 2 in H_2O and a factor of 3.5 in D_2O ,
- (3) the "basic" mechanism in H_2O is significantly impaired by KCl, even at 0.15 M,
- (4) the kinetic H/D isotope effect is 1.6 and 2.7 for the "acidic" and "basic" mechanisms, respectively, and is affected by the addition of 0.15 M KCl.

In the following sections we shall explore the consequences of these and other experimental findings in terms of some simple models for prototropic charge transfer.

3. THE MECHANISM

We will adopt the view, first propounded by Danneel¹ in 1905 and implied in virtually all subsequent models, that the elementary step in prototropic charge transport consists of transfer of a positive or a negative charge between two oxygen atoms[†] connected via a hydrogen bond. This charge relocation is coupled to a proton transfer within the hydrogen bond as shown in fig. 6. (At this stage we are not concerned with the detailed geometry of the molecular environment in which the elementary step takes place. Fig. 6 is intended merely as an illustration of the transition state topology.)

As a basis for classification and formulation of models for prototropic charge transport, we introduce the elementary return probability P_R . This is the probability that the charge returns to the same oxygen atom after two elementary steps. Although intimately related to the dynamics of the transfer process, the probability P_R provides a simpler conceptual basis than do the various characteristic times associated with the process. We can then distinguish between the following three limiting models of transfer:

$$\text{Fluctuation transfer: } P_R = 1 \quad (22a)$$

$$\text{Markovian transfer: } P_R = 1/3 \quad (22b)$$

$$\text{Concerted transfer: } P_R = 0 \quad (22c)$$

These limiting cases will now be discussed in turn. (Unless otherwise stated, all considerations will be assumed to apply also to the deuterated species.)

[†] In the H_3O^+ ion, the excess positive charge is of course not localized at the oxygen atom. However, since the charge is symmetrically distributed with respect to the oxygen atom, it is convenient to think of the charge as being transferred from one oxygen atom to another.

3.1 FLUCTUATION TRANSFER

It is now firmly established^{41,53,54} that the primary charged prototropic entities in aqueous solution are the hydronium ion H_3O^+ , with C_{3v} symmetry, and the hydroxide ion OH^- . In sufficiently dilute aqueous solution the hydronium ion donates three strong (250 pm) H-bonds to adjacent water molecules.[†] We further assume that the hydroxide ion acts as an acceptor of three strong H-bonds.[#] A prototropic charge can thus be transferred via either of three H-bonds, accounting for the 1/3 in the definition (22b). We shall assume that this H-bond topology obtains at all temperatures of interest.[¶]

Extremely rapid (frequency 10^{13} - 10^{14} s^{-1}) proton transfer within the hydrated prototropic ion complexes has been postulated by several

[†] The diffraction data⁴¹ revealed four nearest-neighbor oxygen atoms around H_3O^+ , but the orientation of the fourth ligand could not be ascertained. However, according to ab initio calculations¹⁰ on $\text{H}_3\text{O}^+(\text{H}_2\text{O})_4$, a charge-dipole interaction is essentially thermoneutral (relative to infinite separation of the fourth ligand), whereas a fourth H-bond is strongly repulsive. It is thus reasonable to assume that the aqueous H_3O^+ ion is involved in only three H-bonds.

[#] There are no diffraction data available for the hydrated OH^- ion. However, ab initio calculations⁹ have shown the triply H-bond-accepting OH^- ion to be the most stable configuration of $\text{OH}^-(\text{H}_2\text{O})_3$.

[¶] The binding energy of the third water in $\text{H}_3\text{O}^+(\text{H}_2\text{O})_3$ and in $\text{OH}^-(\text{H}_2\text{O})_3$ is^{9,10,55,56} on the order of 100 kJ mol^{-1} , i.e., ca. 20 kT even at 600 K.

authors; most notably by Eigen and De Maeyer⁶ and by Zundel and coworkers.⁵⁷ Indeed, accurate CI-level quantum-mechanical calculations on the systems H_5O_2^+ (ref. 11) and H_3O_2^- (ref. 12) indicate flat symmetric single-minimum (no barrier) potentials for proton transfer in the minimum-energy configurations of the isolated species. However, there is no evidence for the existence of these species in aqueous solution over times longer than their vibrational periods. Moreover, in their extensive ab initio study⁹ Newton and Ehrenson found that fluctuation transfer within the $\text{H}_3\text{O}^+(\text{H}_2\text{O})_3$ and $\text{OH}^-(\text{H}_2\text{O})_3$ complexes are strongly endothermic processes. Thus, one expects charge transfer to proceed mainly between equally hydrated sites, i.e. to water molecules which are already engaged in H-bonds to two further water molecules. But then, according to (22), we have Markovian rather than fluctuation transfer.

The Eigen-De Maeyer postulate⁶ of rapid fluctuation transfer was based largely on two experimental results: (1) the inability to detect the H_3O^+ ion by vibrational spectroscopy and (2) the two orders of magnitude larger prototropic mobility in ice compared to liquid water. Today these arguments are no longer valid; the infrared spectrum of H_3O^+ in aqueous hydrohalic acids has been recorded⁵³ and the prototropic mobility in ice is now believed to be lower than in the liquid state.⁵⁸

Fluctuation transfer, even if it occurred, could not be the whole story. This is because fluctuation transfer does not, on the average, produce any net charge displacement and consequently cannot account for the large prototropic contribution to the electric conductivity of aqueous solutions. In fact, the charge delocalization associated with fluctuation transfer would increase the effective size of the migrating ion and hence reduce its mobility. Furthermore, fluctuation transfer cannot explain the observed scalar relaxation

since it is the same proton which is being traded back and forth.[†]

3.2 MARKOVIAN TRANSFER

Markovian transfer obtains when the charge-accepting oxygen atom is essentially equivalent to the charge-donating oxygen atom with respect to H-bonding. Prototropic charge transfer then proceeds as a Markov chain with transition probability 1/3 to each of the three H-bonded oxygen atoms, independently of the previous elementary step.

The two most extensively discussed models for prototropic charge transport in water, namely those due to Conway, Bockris, and Linton⁵ and to Eigen and De Maeyer⁶, both take "structural diffusion" involving water reorientation to be rate-limiting, rather than the proton jump itself. The two models differ, however, as to whether the structural diffusion is effected by the primary (Conway, Bockris, and Linton) or by the secondary (Eigen and De Maeyer) hydration waters.

It might be argued that these structural diffusion models are inconsistent with experimental data in the following two respects: (1) the mean lifetime of an H_3O^+ ion is 1.3 ps (sect. 4), while

[†] This is true for the three water molecules in the complexes $\text{H}_3\text{O}^+(\text{H}_2\text{O})_3$ and $\text{OH}^-(\text{H}_2\text{O})_3$. On the other hand, if fluctuation transfer occurred, the central oxygen atom would exist transiently as part of a water molecule, the two protons of which would be "scrambled" among the three H-bonded protons. However, in the experimentally interesting pH range, the fraction of such water molecules would be so small ($\lesssim 10^{-7}$) that their contribution to the observed relaxation behavior would be completely negligible.

the water dipole rotational correlation time is^{19,20,59} 7.2 ps, and (2) the Arrhenius activation energy for proton transfer is⁵¹ 10 kJ mol⁻¹, to be compared with²⁰ 19 kJ mol⁻¹ for water reorientation. These figures refer to 28°C and, in the case of water reorientation, to bulk water. We do not believe (see sect. 4.2) that both of these inconsistencies can be removed by postulating⁵ a strongly accelerated water rotation due to the electrostatic torque in the ionic field.

On the basis of ab initio calculations on $\text{H}_3\text{O}^+(\text{H}_2\text{O})_5$, Newton¹⁰ has proposed a mechanism for prototropic charge transport which avoids the inconsistencies in the structural diffusion models. The essence of Newton's argument is that bond-length reorganization (rather than water reorientation) within a more or less strongly H-bonded environment limits the rate of prototropic charge transport. The basic features of this mechanism are illustrated in fig. 7 (which is an adaption of fig. 8 of ref. 10).

IG. 7
A hydronium ion with three short primary H-bonds and two relatively short secondary H-bonds is transformed, by means of bond-length reorganizations, into a symmetric, strongly H-bonded $(\text{H}_2\text{O})_2(\text{H}_5\text{O}_2^+)(\text{H}_2\text{O})_2$ configuration. The activation energy for prototropic charge transport consists of the energy difference between these two structures (in their aqueous environment). The proton is then transferred within the central short H-bond in the activated complex at no extra energy cost (and with no need for tunneling), whereupon a new $\text{H}_3\text{O}^+(\text{H}_2\text{O})_3(\text{H}_2\text{O})_2$ configuration emerges with the charge now residing at a new oxygen atom. This process can evidently be classified as a Markov chain ($P_R = 1/3$). The transport of negative charge may be visualized in a completely analogous manner.

3.3 CONCERTED TRANSFER

The current view of the structure of liquid water has been summarized by Stillinger⁸ as "a macroscopically connected, random network of hydrogen bonds, with frequent strained and broken bonds, that is continually undergoing topological reformation". The H-bonded network topology has been emphasized in several recent theoretical models and computer simulations of liquid water^{8,60-62}. The question

thus presents itself as to whether the extensive H-bond connectivity in liquid water has any consequences for the mechanism of prototropic charge transport and, in particular, whether concerted proton transfer plays a significant role⁷.

Concerted proton transfer in liquid water was actually considered as far back as half a century ago^{4,63,64}. Due to the limited structural knowledge about liquid water at that time, however, these early models have lost their quantitative relevance. More recently, the question of concerted proton transfer has been addressed with quantum-mechanical methods by Fang and coworkers⁶⁵ and by Scheiner¹³. The former authors⁶⁵ performed semiempirical calculations on the system $\text{H}_3\text{O}^+[\text{H}_2\text{O}(\text{H}_2\text{O})_2]_3$ with ice-like geometry and found proton transfer modes (strongly coupled to oxygen lattice modes) involving correlated motion over two H-bonds (which was the maximum correlation range in their system). Due to the ice-like geometrical constraint, however, these results are not directly applicable to liquid water.

Scheiner¹³ performed ab initio calculations on the proton transfer potential surface for the two central H-bonds in the linear system $(\text{H}_2\text{O})_2\text{H}_3\text{O}^+(\text{H}_2\text{O})_2$ and concluded that "once enough energy has been harnessed to achieve the transition state which involves partial transfer of one proton, the transfer of a second proton may be coupled to the completion of the transfer with no additional expense in energy". [Note that the two central H-bonds were fixed at rather large inter-oxygen separations (295 pm) in order to model the longer H-bonds occurring in proteins.]

IG. 8

In fig. 8 we have illustrated a possible concerted proton transfer pathway involving two H-bonds. The configuration shown is somewhat different from that studied by Scheiner - here the charge travels between two energetic "sinks" provided by triply H-bonded oxygen atoms via a doubly H-bonded oxygen atom.

While no quantum-mechanical calculations have been reported for systems of sufficient size to permit concerted proton transfer over more than two H-bonds, it is conceivable that the proton "correlation length" is longer. A necessary, albeit not sufficient, condition for concerted proton transfer is the existence of H-bonded chains. It is thus of some interest to investigate the topology of such chains in liquid water. This we do in appendix A - here we shall only discuss the main results.

A proton transfer chain - in contrast to a H-bonded chain in general - has direction. Starting on a given prototropic ion, e.g. a H_3O^+ ion as in fig. 8, the positive charge migrates along the chain from H-bond donor to H-bond acceptor. What, then, puts an end to this concerted proton hopping? We believe that there are two major causes of chain termination. First, a transfer chain must obviously stop at a dead-end (O_4 and O_5 in fig. 8), i.e. at an oxygen atom with no donor bond (in the case of positive charge transport). Second, a transfer chain can be terminated at an energetic sink (O_3 in fig. 8), i.e. at an oxygen atom with two donor bonds (in the case of positive charge transport). Upon arrival of the positive charge, the sink oxygen becomes equivalent to the starting point - the triply hydrated hydronium ion $\text{H}_3\text{O}^+(\text{H}_2\text{O})_3$.

The topological treatment (appendix A) contains two parameters: the sink-termination probability p_s and the H-bond probability p . The quantity p_s is self-explanatory; for $p_s=0$ all chains are terminated by dead-ends, whereas for $p_s>0$ there is a finite probability of chain termination at a sink site encountered prior to a dead-end. The H-bond probability p is, in the absence of bond correlation (see below), equal to one fourth of the mean number $\langle n \rangle$ of H-bonds per oxygen atom. The quantity p , which depends on temperature, density, isotopic composition, presence of solutes, etc., has been deduced from experiment^{66,67}, in particular from vibrational spectra, and from computer simulations⁶⁰. A H-bond in liquid water can be defined in several ways, e.g., on the basis of the water-water interaction energy, various geometrical criteria, or vibrational frequency shifts. In each case

there is an element of arbitrariness involved in the quantitative H-bond definition and consequently a wide range of p values have been reported. However, it seems safe to assume that, at ambient temperature: $0.5 < p < 0.9$ (cf. also sect. 4.5).

IG. 9

Fig. 9 shows the calculated (appendix A) mean number $\langle N \rangle$ of oxygen atoms in a proton transfer chain [mean number of bonds = $\langle N \rangle - 1$] as a function of the H-bond probability p , for several values of the sink-termination probability p_s . In the range of reasonable p values, sink-termination clearly has a profound effect on the chain length. (Note the different scales in fig. 9.)

As suggested many years ago⁶⁸ and subsequently verified through quantum-mechanical calculations¹⁴, hydrogen bonding in water is a cooperative phenomenon. Of particular importance in the present context is the fact that the three-molecule nonadditivities depend on the polarity of the H-bonds involved. Thus, at interoxygen separations of 300 pm, Hankins et al.¹⁴ calculated nonadditivities (kJ mol^{-1}) of -2.4 (sequential trimer), 2.5 (double donor trimer), and 1.6 (double acceptor trimer). This trend is expected to be even more pronounced due to polarization of the water molecule electron distribution in the field of a prototropic ion. The effect of this H-bond polarity correlation was taken into account in our topological model (appendix A) by requiring all doubly H-bonded chain oxygens to be sequentially bonded (one donor bond and one acceptor bond).[†]

[†] For dead-end chains, polarity correlation affects only the doubly H-bonded oxygen atoms (2-sites), since 3- and 4-sites propagate the chain with unit probability irrespectively of the polarity correlation. For sink-terminated chains, however, there is also a "second-order" polarity correlation effect for 3-sites, due to the different nonadditivities for double donors and double acceptors. This effect, which has been neglected, increases the mean chain length slightly compared to the curves in fig. 9.

Fig. 9. shows the effect of polarity correlation on the mean chain length for $p_s=0$ and $p_s=1$. As expected, the correlation increases the chain length, although the effect is small in the sink-terminated case ($p_s=1$).

There exists in liquid water also a bond correlation, i.e., the H-bond probability p for a given oxygen atom depends on the number of H-bonds that it is engaged in. Thus, p is not strictly equal to $\langle n \rangle / 4$. Qualitatively, the effect of bond correlation should be the same as from an increased (relative to $\langle n \rangle / 4$) effective p value. In view of the substantial experimental uncertainty in this quantity, we have not deemed it worthwhile to incorporate bond correlation into the topological model .

Finally, we should mention a third mode of chain termination, which may be called correlation damping. Although proton transfers may be nearly perfectly correlated ($P_R=0$) over two or three bonds, long-ranged concerted transfer processes must be accompanied by successive dissipation of the activation energy (acquired in the initial phase of the process) into the numerous "lattice" degrees of freedom. This phenomenon may be formally described by a sink-termination probability which increases in the direction of the proton transfer chain. However, if p_s is not too low, long concerted chains are improbable (fig. 9) and correlation damping might then never come into play.

4. TEST OF MODELS

In the foregoing section we considered three limiting cases of proton transfer, namely fluctuation transfer, Markovian transfer, and concerted transfer. For each case we proposed underlying mechanisms, the pros and cons of which were discussed mainly on theoretical grounds. In this section we shall test these model mechanisms against experiment.

There are two principal sources of experimental data on prototropic charge transport in aqueous solution: (1) NMR relaxation experiments (sect. 2), which provide the rate constants $k_{\pm}$ [eqn (14) and (15)], and (2) electric conductivity measurements, which give the limiting prototropic molar conductivities $\lambda_{\pm}$ (sect. 4.3). With the aid of some additional theory, the two pairs of quantities k_{+}, λ_{+} and k_{-}, λ_{-} gives us the mean lifetimes $\tau_{\pm}$ of the prototropic ions H_3O^{+} and OH^{-} . These lifetimes are fundamental for the understanding of prototropic charge transport in general and for the elucidation of the rate-limiting step in these processes in particular.

The connections between the lifetimes $\tau_{\pm}$ and the primary experimental quantities - $k_{\pm}$, on the one hand, and $\lambda_{\pm}$, on the other - reflect the underlying mechanism in different ways. By combining NMR and conductivity data, we can thus test the various models for prototropic charge transport. Further tests are provided by the variations in $k_{\pm}$ and $\lambda_{\pm}$ with temperature, pressure, isotopic substitution, electrolyte addition, etc. To begin with, we shall adopt the hypothesis that prototropic charge transport can be described as a Markov chain ($P_R = 1/3$) and investigate whether the quantitative implications of this model are consistent with established experimental facts.

4.1. PROTOTROPIC LIFETIMES FROM NMR

As shown in sect. 2.3, NMR data provide the two rate constants $k_{\pm}$, which are simply related - through definition (15) - to the limiting mean specific exchange rates $r_{\pm}$. These quantities measure the mean number

of exchanges effected by a single prototropic charge in unit time at infinite dilution with respect to prototropic charges. In order to obtain from $r_{\pm}$ the mean lifetimes $\tau_{\pm}$ of prototropic ions, we must recognize that the rates $r_{\pm}$ refer to NMR-active exchanges, i.e., to events whereby one of the water protons is exchanged for a different one.

Imagine that we could label the prototropic charges in the system. We can then say that a given water molecule will, on the average, spend a time τ_{enc} between encounters with differently labeled prototropic charges. However, in the case of Markovian proton transfer, i.e., with an elementary return probability $P_R = 1/3$, only two out of three such encounters will be NMR-active. This follows since upon arrival of a charge, a water molecule is transformed into a triply hydrated H_3O^+ (H_2O)₃ or $\text{OH}^-(\text{H}_2\text{O})_3$. Consequently, the probability is 1/3 that the particular proton which was added to (removed from) the original water molecule will also be the one to be lost (gained) as the charge continues on its journey. The encounter time is thus shorter than the exchange time by factor 2/3,

$$\tau_{\text{enc}} = \frac{2}{3} \tau_{\text{exc}} . \quad (23)$$

Ever since Meiboom's pioneering work¹⁵, the occurrence of NMR-inactive proton exchanges has been recognized by explicitly introducing a factor 2/3 (or 1/3 in the case of ¹H NMR) in eqn (14), but only in the term associated with positive charge transport[†]. This neglect of the symmetry between

[†] In this connection it should be pointed out that the recent⁶⁹ suggestion that, by definition, $k_+ = k_-$ (or $k_1/k_2 = 3/2$ in the conventional nomenclature) is incorrect. This equality was derived under the erroneous assumption that the concentration c_+^* , corresponding to the minimum in $1/\tau_{\text{exc}}$, is also the minimal c_+ . That this is not generally true is seen from our eqn (20).

positive and negative charge transfer may stem from viewing the H_3O^+ and OH^- ions in isolation, while, in fact, they are each involved in three strong H-bonds. (If this were not so, the factor $2/3$ would not be correct even for H_3O^+ , since then the probability for the incoming proton to be also the outgoing one would exceed $1/3$.) Our argument, of course, requires the three H-bonds to remain intact during the lifetime of the ion. That this must indeed be the case follows from the fact that the prototropic ion lifetimes (table 5) are about one order of magnitude shorter than either the residence time or the re-orientation time for water molecules similarly closely attached to (non-prototropic) ionic species⁷⁰. Previously reported rate constants for negative charge transport should thus be multiplied by a factor $3/2$. (This correction has been included in our comparison with previous results in table 4.)

Equation (23) relates the exchange time τ_{exc} , which determines the scalar relaxation rate, to the mean time τ_{enc} spent by a given oxygen atom between encounters with differently labeled prototropic charges. The mean encounter time τ_{enc} depends on the concentration of prototropic ions - in neutral water it is on the order of 1 ms. To obtain from τ_{enc} the mean lifetimes $\tau_{\pm}$ of prototropic ions, we must take into account the fact that, during a short time after an encounter between a given oxygen atom and a given prototropic charge, the re-encounter probability is significant. While this is a well-known phenomenon in the theory of diffusion-controlled chemical reactions⁷¹, it has apparently been neglected in connection with prototropic charge transport. As soon as one recognizes the H-bonded structure of liquid water, it becomes clear that the inequality of τ_{enc} and τ_{exc} , as expressed in eqn (23), is nothing but a "first-order" correction for re-encounter events. (Re-encounters in Markovian proton transfer should not be confused with fluctuation transfer.)

The problem, then, is to calculate the time-dependent probability that a given oxygen atom and a given prototropic charge, separating from an encounter, will re-encounter each other. In other words: we want to

know the mean number $\gamma(N)$ of re-encounters after N proton transfer steps. A certain period of time, which we may call the dwell time, after the original encounter, the re-encounter probability will essentially have reached its statistical (time-independent) value, which, of course, is vanishingly small for any macroscopic system[†]. At the same time $\gamma(N)$ will have approached its limiting value $\gamma \equiv \gamma(N \rightarrow \infty)$, i.e., the mean total number of re-encounters.

FIG. 10

In appendix B we calculate the quantity $\gamma(N)$ for Markovian proton transfer on a model lattice. The result is shown in fig. 10. We see that $\gamma = 1$, i.e., a given prototropic charge will, on the average, encounter each oxygen atom twice on its random trajectory through the system. From fig. 10 we can also infer that practically all re-encounters occur during a dwell time on the order of $10 \tau_{\pm}$ (cf. $\tau_{\pm}$ in table 5), during which time the charge remains within a few H-bonds from the reference oxygen atom. We are thus probably justified, at least for H_2O (see below), in assuming that the H-bonds of the re-created prototropic ion involve the same three protons as the original ones. In that case, all re-encounters - not just the two-step re-encounters considered in eqn (23) - will be NMR-inactive[#]. Consequently, the mean prototropic

[†] In a sample of $1 \text{ cm}^3 H_2O$ at $28^\circ C$, a given oxygen atom has to wait, on the average, some 2700 years to encounter again a given positive charge, which has just escaped from the immediate neighborhood of the reference oxygen atom.

[#] Re-encounters leading to prototropic ions which are H-bonded to the same three protons as the original ion are NMR-inactive, i.e. they do not contribute significantly to the scalar relaxation rate. This can be seen by regarding the successive re-encounters as a single exchange event, the duration of which is short compared to τ_{exc} , as

lifetimes $\tau_{\pm}$ are given by

$$\frac{1}{\tau_{\pm}} = (1 + \gamma) r_{\pm} = (1 + \gamma) k_{\pm} c_w, \quad (24)$$

where the second equality follows from eqn (15).

TABLE 5

Mean lifetimes for prototropic ions, calculated according to eqn (24) with $\gamma = 1$ and rate constants from table 3, are given in table 5. Our value of 1.27 ± 0.06 ps for the mean lifetime of an aqueous H_3O^+ ion may be compared to previous estimates of 0.24 ps by Conway, Bockris, and Linton⁵ and of 0.25 ps by Gagliardi⁷². Conway et al. base their estimate on a classical-mechanical calculation of the time taken for a water dipole to rotate in the field of an H_3O^+ ion (this was assumed by the authors to be the rate-limiting step). This is a very crude approach and can hardly be taken quantitatively. Gagliardi derived his value from conductivity data using a value of 150 pm for the elementary proton transfer distance. This value, which was selected rather arbitrarily, is, in our opinion, unreasonably small[†].

required for eqn (6) to be valid. Alternatively, we may consider the power spectrum (which is proportional to the scalar relaxation rate¹⁸) for proton exchange. This can be written as the sum of two terms: one related to re-encounters with the same charge and the other related to encounters with different charges (assuming that they were labeled). However, the first term is negligible on account of the short correlation time for re-encounters (dwell time $\lesssim 10^{-11}$ s) compared to τ_{exc} ($\gtrsim 10^{-5}$ s in the experimentally interesting pH range), which is the correlation time for the second term.

[†] Gagliardi⁷² also performs an angular integration, the significance of which is not clear to us.

The longer prototropic lifetimes for the deuterated species (table 5) imply that the dwell time is correspondingly longer in D_2O . Consequently, the D-bond configuration around a reference oxygen atom might be altered during the time between the original encounter and a subsequent re-encounter. The probability of exchange events whereby both deuterons are exchanged might then become non-negligible. Although we have not derived an expression for the ^{17}O lineshape including the possibility of two-spin exchanges, we believe that this effect could be responsible for the deviations in the fits to the D_2O data (fig. 4 and 5).

In concluding this subsection, we consider the mean lifetime of a water molecule, i.e., the mean time between events whereby a water molecule is transformed into a prototropic ion. From the preceding discussion it is clear that these events occur, on the average, in pairs. The "duration" of a pair is on the order of the dwell time (ca. $10 \tau_{\pm}$), whereas the time between different pairs, which we denote by τ_w , equals the exchange time τ_{exc} . Thus, from eqn (14) and (19),

$$\frac{1}{\tau_w} = \left(\frac{k_+}{\alpha_+} 10^{-pH} + \frac{k_-}{\alpha_-} 10^{pH} \right) . \quad (25)$$

FIG. 11

Fig. 11 shows τ_w versus pH for pure H_2O and D_2O according to eqn (25) with $\alpha_{\pm}$ and $k_{\pm}$ from tables 2 and 3, respectively. Outside the neutral region ($6.0 \lesssim pH \lesssim 8.2$) either H_3O^+ or OH^- catalyzed proton exchange dominates and $\log \tau_w$ depends linearly on pH according to the relations given in fig. 11. Note that eqn (25) and our results for τ_w are model-independent. (The occurrence of pairs of O-H bond disruptions, however, is a prediction of the Markovian transfer model.)

4.2. DYNAMIC ASPECTS OF PROTOTROPIC HYDRATION

Prototropic ions differ from other ions primarily through their finite lifetime — a fact which must be borne in mind when discussing their interaction with the surrounding aqueous medium. Except for two

papers (published in 1973-4) by Gagliardi^{72,73}, little attention has been given to the important question: Do prototropic ions have time to become hydrated?

At first thought, one might be tempted to answer this question in the negative, considering our value of 1.3 ps for the H_3O^+ lifetime (table 5) and the value (also referring to 28°C) of 7.2 ps for the water dipole rotational correlation time (sect. 3.2). However, the structural relaxation of the first few water neighbours must be strongly influenced by the ionic field. According to dielectric continuum theory⁷⁴, the characteristic time for polarization of the dielectric medium around an instantaneously created charge is $\tau_d \epsilon_\infty / \epsilon_s \approx 0.4$ ps. Here τ_d is the conventional dielectric relaxation time in a constant external field, while ϵ_r and ϵ_∞ are the static and high-frequency permittivities⁵⁹.

Molecular models tend to give even shorter relaxation times. Thus Conway, Bockris, and Linton⁵ calculate (rather crudely) that a 120° rotation of a water molecule in the field of an H_3O^+ ion requires merely 0.024 ps. Note, however, that the initial state was taken as a highly repulsive (ca. 200 kJ mol⁻¹) "D-defect" configuration. A more realistic approach was taken by Rao and Berne (although they did not have prototropic charge transfer in mind) in a recent⁷⁵ molecular dynamics simulation of the water relaxation process around an equilibrated neon atom upon instantaneous "ionization" to charge +2. According to this study, the rotational relaxation of the first solvent shell is essentially complete within 0.07 ps of the ionization. Then follows a rapid "electrostriction" (shortening of the ion-oxygen distances) completed ca. 0.2 ps after ionization. No significant structural changes occur during the remainder of the 0.6 ps simulation run.

If, despite the, in some cases, rather severe approximations involved, we accept the order of magnitude of the aforementioned results, should we then conclude that prototropic ions do indeed become hydrated during

their brief lifetime? We think not. More precisely, we believe that the prototropic charge migrates preferentially to "prehydrated" sites, i.e., to water molecules which donate (in the case of positive charge transport) two H-bonds even before the excess proton arrives (cf. sect. 3). The third H-bond in the $\text{H}_3\text{O}^+ (\text{H}_2\text{O})_3$ complex is formed "automatically" through the polarity reversal accompanying the proton jump. Thus there is no need for water reorientation. During the 1.3 ps H_3O^+ lifetime, the three primary H-bonds remain intact, thus preventing rotation, while H-bond vibrations and librations (with periods in the range 0.05 - 0.5 ps, according to vibrational spectra⁶⁷) relax the local environment. Consequently, the highly non-equilibrium initial states, which obtain in the aforementioned situations, never occurs for aqueous prototropic ions. In other words: the prototropic ion cannot pay the high energetic price to achieve those particular configurations (referred to as "hot spots" by Rao and Berne) that are most efficient in accelerating water reorientation. The occurrence of such high-energy configurations is not consistent with the observed⁵¹ low activation energy (10 kJ mol^{-1} , corresponding to one half of a typical H-bond between neutral species) for proton transfer in liquid water.

The hydration of prototropic ions thus appears to be distinct from that of other ions. According to our prehydration concept, prototropic charges reside preferentially at sites in the water "lattice" which have a sufficient number of H-bonds of the required polarity. The surrounding water structure is perturbed to the extent that (1) there are three primary H-bonds, of the same polarity, to the prototropic oxygen and (2) these "H-bonds" are much stronger than those between neutral water molecules. On energetic grounds, we expect that the prehydration requirements are essentially satisfied by the primary "hydration shell". Furthermore, there should be very little field-induced perturbation of water structure outside of the primary shell, since the time lag in the orientational polarization process exceeds the lifetime of the prototropic ion. Prototropic ions should thus exhibit little or no secondary and further hydration (in the sense of perturbation of the bulk water structure). This conclusion was reached also by Gagliardi⁷³, although his view of the primary prototropic hydration differs from ours.

The weak long-range part of the ion-solvent interaction is not expected to contribute significantly to bulk thermodynamic properties. Thus H_3O^+ and OH^- behave as other ions of similar size with respect to enthalpies of hydration, partial molal volumes, partial molal heat capacities, etc.⁷⁶. However, there exist several subtle phenomena, e.g., dielectric friction (sect. 4.3) and hydration forces, which are thought to originate in the weak long-range tail of the ion-solvent interaction.

The hydration force is an experimentally well-established^{16,77-79} repulsive component in the force between various types of surfaces immersed in aqueous media. This force, which decays exponentially with characteristic lengths in the range 0.2 - 1.5 nm, cannot be accounted for by the conventional DLVO-theory. Rather it is thought to be a manifestation of the long-range tail of the surface-solvent and/or counterion-solvent interaction. In an extensive study of the hydration force between mica surfaces immersed in various aqueous electrolyte solutions, Pashley⁷⁸ made the interesting discovery that hydration forces are absent when the dominating counterion is H_3O^+ . This was found to be the case also in bubble coalescence experiments⁷⁸. Pashley notes: "Hydration of the H_3O^+ ion must be of a different nature to that of an alkali metal ion, since the position of the proton can be rapidly transferred by a change in water bonding". Our picture of prototropic prehydration devoid of long-range tail clearly supports this suggestion of a dynamic origin of the H_3O^+ -induced inhibition of the hydration force[†].

[†] In a complete description of the system, time does not enter explicitly in expressions for equilibrium properties. Here, however, the time variable serves merely to represent implicitly those interactions that govern the dynamics.

An alternative, although essentially equivalent, explanation of the origin of the hydration force, in terms of continuum theory, has recently been presented (B. Jönsson and H. Wennerström, work in progress). At this level of description, the long-range effect of counterion (or headgroup) hydration appears as an interaction of these charged (or dipolar) species with their image charges (or, equivalently, with the surface charge induced at the dielectric discontinuity). The magnitude (and sign) of these image charges is determined by the (frequency dependent) permittivities of the two media. Because of the high mobility of prototropic charges, and the ensuing lack of long-range orientational polarization, the effective permittivity of the aqueous region will be drastically reduced and so will the repulsive image charges. This effect is somewhat analogous to retardation in the theory of the dispersion force⁸⁰.

4.3. COMPARISON WITH CONDUCTIVITY DATA

The lifetimes reported in table 5 were arrived at by assuming that prototropic charge transport in water can be described as a Markov chain. If this is true, these lifetimes must be consistent with all experimental data relating to prototropic charge transport in water and, in particular, with the electric conductivity.

It is not a trivial matter, however, to deduce a quantitative relationship between the lifetimes $\tau_{\pm}$ and the limiting molar conductivities, $\lambda(\text{H}_3\text{O}^+)$ and $\lambda(\text{OH}^-)$, of the prototropic ions. The source of the problem is that the measured current is carried not only by the excess charge itself, as during the actual proton jump, but also, during the time $\tau_{\pm}$ between successive jumps, by some ill-defined massive kinetic entity comprising the prototropic ion and part of its aqueous environment. It is usually assumed that these two kinds of carrier contribute independently to the observed conductivity, i.e., that

$$\lambda(\text{H}_3\text{O}^+) = \lambda_+ + \lambda_+^S, \quad (26)$$

with a similar relation for $\lambda(\text{OH}^-)$. In eqn (26), λ_+ is the limiting (infinite dilution with respect to prototropic ions) prototropic molar conductivity and λ_+^S is the remaining contribution, which may be termed the Stokesian conductivity. The assumption that λ_+ and λ_+^S refer to independent processes has never been justified theoretically, but arguments, albeit not rigorous, in its favour can be found. As emphasized by Rice and Sceats in their random network model⁶², molecular motions in liquid water occur on two disjoint time scales. Thus the characteristic times for translation and reorientation are 5-10 ps, while intermolecular vibrations and librations have periods in the range 0.05 - 0.5 ps. With these facts in mind, we can envision the prototropic conduction process as occurring on the fast time scale through a H-bonded network, the slower fluctuations of which govern the Stokesian drift. Since it is the network structure that controls the proton jumps (sect. 4.2), rather than the other way around, we can expect the Stokesian process to be dynamically essentially uncoupled from the jump process.

Unfortunately, it does not appear to be possible to measure the Stokesian contribution directly, since the available techniques for measuring self-diffusion coefficients (tracer, NMR pulsed field gradient, scattering) involve too long time scales (relative to $\tau_{\pm}$) and/or are not sensitive enough to yield the limiting diffusion coefficient. Hence one is forced to make additional assumptions. The conventional approach is to identify $\lambda_{\pm}^S$ with the conductivities of non-prototropic ions of the same (crystal) radii as the H_3O^+ and OH^- ions. The natural choices would then be K^+ and F^- †.

† Thermodynamically, however, the H_3O^+ ion behaves more nearly as Na^+ ⁷⁶. Furthermore, due to the limited amount of conductivity data on F^- , it has been the custom to take Cl^- as the negative reference ion.

Because of the transient nature of prototropic ions, this approach is not free from objections. As argued in sect. 4.2, prehydrated prototropic ions exhibit no long-range hydration. One would therefore expect them to have smaller hydrodynamic radii than reference ions of similar crystal radii. For the same reason, prototropic ions should experience little or no dielectric friction⁷², since this force arises from the lag in the polarization induced by the long-range ion-solvent interaction⁸¹. Both of these effects should increase $\lambda_{\pm}^S$ over the reference ion conductivities. In the following, we shall therefore regard the quantities $\lambda_{\pm}^S$ as parameters, the magnitudes of which will be estimated from a comparison of prototropic lifetimes and (total) conductivities in H₂O and D₂O (see below).

Let $D_{\pm}$ denote the limiting prototropic translational diffusion coefficients, which are related to the limiting conductivities $\lambda_{\pm}$ through the Nernst equation

$$D_{\pm} = \frac{RT}{F^2} \lambda_{\pm} \quad (27)$$

This relation is subject only to the limitations of linear response theory⁸². This means, in particular, that we assume the mechanism of prototropic charge transport to be unaffected by the external field applied during a conductivity measurement.

For a Markov process in an isotropic system, the diffusion coefficients $D_{\pm}$ are related to the lifetimes $\tau_{\pm}$ through the Einstein equation⁸³

$$6 D_{\pm} \tau_{\pm} = \sigma_{\pm}^2 \quad (28)$$

where $\sigma_{\pm}$ are the isotropically distributed root-mean-square (rms) displacements occurring with frequency $1/\tau_{\pm}$. In sect. 3, Markovian transfer was defined solely on the basis of the elementary return probability, as the case of $P_R = 1/3$. More rigorously, we must require

of a Markovian proton transfer process that the direction and length of a given elementary step are completely uncorrelated with those of the previous one⁸⁴. Since a prototropic ion does not reorient appreciably during its lifetime, the requirement for a Markov process is satisfied only if $P_R = 1/3$ and if the three primary H-bonds lie in a plane. The latter condition is assumed to be very nearly satisfied.

FIG. 12

On combining eqn (26) - (28), we obtain a relation containing two unknowns: $\sigma_{\pm}$ and $\lambda_{\pm}^S$. In fig. 12 we have displayed these relations graphically for H_3O^+ , OH^- , D_3O^+ , and OD^- . We have used lifetimes from table 5 and limiting molar conductivities (at 28.0°C) from the literature[†]. To proceed, we shall make two assumptions: (1) there is no isotope effect on the elementary step lengths $\sigma_{\pm}$, and (2) the Stokesian conductivities $\lambda_{\pm}^S$ follow Walden's rule, i.e., they are inversely proportional to the shear viscosity of the medium. If the first assumption is taken to imply only that the oxygen-oxygen distances in the transition state configurations $H_5O_2^+$ and $H_3O_2^-$ are the same as in the deuterated species, then it is surely an excellent approximation[#]. The second assumption holds true, within a few percent, for non-prototropic ions⁸⁹ with respect to the solvent isotope effect at 25°C. Thus, if we maintain that the Stokesian contributions $\lambda_{\pm}^S$ are similar in nature to the conductivity of non-prototropic ions, then we must require that $\lambda_{\pm}^S(H_2O)/\lambda_{\pm}^S(D_2O) = \eta(D_2O)/\eta(H_2O) = 1.22$ at 28°C.

The consequences of imposing these two constraints are shown by the horizontal lines in fig. 12. The resulting step lengths $\sigma_{\pm}$ are suspiciously

[†] $\lambda(H_3O^+) = 364.0$ was obtained from ref. 46, $\lambda(OH^-) = 206.0$ from ref. 85, $\lambda(D_3O^+) = 261.6$ and $\lambda(OD^-) = 121.5$ from ref. 86, using a transport number $t(Na^+) = 0.40$ (ref. 46). All data at 28.0 °C and in units of $S\ cm^2\ mol^{-1}$.

[#] Diffraction data on crystals⁸⁷ as well as theoretical considerations⁸⁸ show that deuteration leads to a slight ($\lesssim 0.5$ pm) contraction of short single-minimum H-bonds, whereas longer double-minimum H-bonds are lengthened by a small ($\lesssim 2$ pm) amount.

short, while the Stokesian conductivities $\lambda_{\pm}^S$ far exceed those of non-prototropic ions of similar size[†]. Taking into account the uncertainty in our lifetimes (for prototropic ions), we obtain, from fig. 12, the following limits:

$$191 \leq \sigma_{-}/\text{pm} \leq 228$$

$$87.0 \leq \lambda_{-}^S(\text{H}_2\text{O})/\text{S cm}^2 \text{ mol}^{-1} \leq 115.7 .$$

For $\text{H}_3\text{O}^+/\text{D}_3\text{O}^+$ we find $\sigma_{+} = 187 \text{ pm}$ and $\lambda_{+}^S(\text{H}_2\text{O}) = 193 \text{ S cm}^2 \text{ mol}^{-1}$ - however, the uncertainties in these figures are large owing to the similar slopes of the H_3O^+ and D_3O^+ curves.

Whereas the large values for $\lambda_{\pm}^S$ perhaps could be explained by low hydration and absence of dielectric friction, the small $\sigma_{\pm}$ values are indeed puzzling. The best quantum-mechanical calculations^{11,12} yield oxygen-oxygen separations of 239 and 246 pm for the (isolated) species H_5O_2^{+} and H_3O_2^{-} , respectively[#]. Although the potential curves versus O-O separation are rather flat near the minimum[¶], the low

[†] From ref. 46, we find for the limiting molar conductivity ($\text{S cm}^2 \text{ mol}^{-1}$) in H_2O at 28°C : 41.5 (Li^{+}), 53.5 (Na^{+}), 77.9 (K^{+}), 81.7 (Cs^{+}), 58.9 (F^{-}), 81.1 (Cl^{-}), 82.9 (Br^{-}), 81.5 (I^{-}). From the self-diffusion coefficient⁹¹ of H_2O we may compute, by eqn (27), a "conductivity" of $91.8 \text{ S cm}^2 \text{ mol}^{-1}$ at 28°C .

[#] Diffraction data⁹² from a variety of acid crystal hydrates yield an average O-O separation in H_5O_2^{+} of $244 \pm 2 \text{ pm}$.

[¶] According to ref. 12, a shortening of the oxygen-oxygen distance in H_3O_2^{-} from 246.5 pm (equilibrium) to 238.1 pm costs a mere 1.66 kJ mol^{-1} .

activation energies⁵¹ for prototropic charge transport are probably inconsistent with oxygen-oxygen distances shorter than 220 pm (H_5O_2^+) and 230 pm (H_3O_2^-). Moreover, the effective step lengths $\sigma_{\pm}$ are likely to exceed the oxygen-oxygen distances in the transition states, due to the bond length relaxation induced by the charge displacement. It should be noted also, that any deviation from the Einstein equation (28), due to correlated motion (with $P_R = 1/3$), would lead to even shorter calculated step lengths $\sigma_{\pm}$.

The conclusion from this analysis in terms of the Markovian model must be that the Stokesian contributions $\lambda_{\pm}^S$ to the conductivities are in fact not Stokesian, i.e., they are not inversely proportional to viscosity. If we set $\lambda_{\pm}^S(\text{H}_2\text{O})$ equal to the K^+ and F^- conductivities, then the H_3O^+ and OH^- curves in fig. 12 yield the entirely reasonable values $\sigma_+ = 242$ pm and $\sigma_- = 248$ pm. Then, however, we must also conclude that there is no significant solvent isotope effect on $\lambda_{\pm}^S$.

4.4. CONCERTED TRANSFER

The previous treatment, valid for Markovian proton transfer, must be amended in several respects in order to include the possibility of concerted processes. The distinction between Markovian and concerted transfer is meaningful only if, in the latter case, the time spent by the prototropic charge at sequential sites (e.g. O_2 in fig. 8) is much shorter than its lifetime at a terminal site. Just as we regarded the Markovian transfer steps as instantaneous, we shall regard concerted transfer chains as occurring instantaneously, i.e., in perfect concert ($P_R = 0$). This limiting case may be relevant if the mean chain length $\langle N \rangle$ is short.

In the reasonable range of H-bond probabilities p (at ambient temperature), nearly all chains will be sink-terminated (fig. 9), provided that the sink-termination probability p_s is not very close to zero. Under these

conditions, the probability for an NMR-active exchange event is 2/3 for the initial site and unity for all sequential sites in the chain. (The final site is counted as initial site in the ensuing chain.) Equation (23) thus generalizes to

$$\tau_{\text{enc}} = \left[1 - \frac{1}{3(\langle N \rangle - 1)} \right] \tau_{\text{exc}} , \quad (29)$$

which reduces correctly in the Markovian limit ($\langle N \rangle = 2$).

The problem of re-encounters is considerably more complicated in the non-Markovian case. However, since the re-encounter probability decreases rapidly as the charge recedes from a given oxygen atom (appendix B), it seems reasonable to neglect, for concerted processes, re-encounters requiring more than two steps. The consequent underestimation of NMR-inactive exchange events is cancelled, to some extent, by neglecting also the possibility of "un-doing" NMR-active proton exchanges at sequential sites through immediate chain reversal. In place of eqn (24), we thus write

$$\frac{1}{\tau_{\pm}} = \left[1 - \frac{1}{3(\langle N \rangle - 1)} \right]^{-1} k_{\pm} c_w , \quad (30)$$

where $1/\tau_{\pm}$ is the mean frequency of individual proton jumps. The time taken for a prototropic charge to traverse an average chain of $\langle N \rangle$ oxygen atoms is $(\langle N \rangle - 1)\tau_{\pm}$. Since, by assumption, the residence time of the charge at sequential sites is zero, the mean lifetimes of (terminal) prototropic ions are given by

$$\tau_{\pm} = (\langle N \rangle - 1)\tau_{\pm} = \frac{\langle N \rangle - \frac{4}{3}}{k_{\pm} c_w} . \quad (31)$$

Resulting lifetimes, for $\langle N \rangle = 3, 4$ or 5 , are given in table 6.

In the case of concerted transfer, eqn (28) should be replaced by

$$6 D_{\pm} \tau_{\pm} = L_{\pm}^2, \quad (32)$$

where $L_{\pm}$ are the isotropically distributed rms displacements occurring with frequency $1/\tau_{\pm}$. The displacement vectors, with rms lengths $L_{\pm}$, are now defined by the terminal sites of each transfer chain. If we make the reasonable assumption that the direction and length of a given chain are uncorrelated with those of the previous one, then we may treat the process as Markovian at the chain level and eqn (32) is valid.

In relating the rms chain lengths $L_{\pm}$ to the elementary displacements $\sigma_{\pm}$, we can make use of some results from the theory of polymer statistics⁹³. If a proton transfer chain involving N oxygen atoms could be described as a random flight, i.e., as a freely jointed chain devoid of all angular constraints, then we would have simply

$$(L_{\pm}^2)_N = (N - 1) \sigma_{\pm}^2 \quad (33)$$

In a real proton transfer chain, however, there is correlation between H-bond directions. If we assume that the dihedral H-bond angles in the chain are random[†], we have a so-called freely rotating chain. For such a chain, composed of N oxygen atoms, one finds⁹³

$$(L_{\pm}^2)_N = (N-1) \left[\frac{1+\alpha}{1-\alpha} - \left(\frac{2\alpha}{N-1} \right) \frac{1-\alpha^{N-1}}{(1-\alpha)^2} \right] \sigma_{\pm}^2. \quad (34)$$

[†] This should be an excellent approximation, since the potential curve for dihedral rotation is very flat in the water dimer⁹⁴ as well as in the $H_5O_2^+$ and $H_3O_2^-$ species⁹.

Here $\alpha \equiv \cos(180-\theta)$, θ being the angle between two adjacent H-bonds in the chain. We shall investigate the tetrahedral ($\theta = 109.47^\circ$, $\alpha = 1/3$) and the planar trigonal ($\theta = 120^\circ$, $\alpha = 1/2$) cases, the real situation being somewhere in between[†]. Finally, we average over the chain distribution

$$L_{\pm}^2 = \sum_{N=2}^{\infty} P(N) (L_{\pm}^2)_N. \quad (35)$$

The probability $P(N)$ is obtained from appendix A as a function of the H-bond probability p and the sink-termination probability p_s .

On combining eqn (26), (27), (31), (32), (34), (35), (A1), (A4), (A5), and (A10) - with the last equation modified to include polarity correlation - we obtain a $\sigma_{\pm} - \lambda_{\pm}^S$ relation containing the three parameters α , p , and p_s . In fig. 13 we have plotted these relations, for the four prototropic species, and with $\alpha = 1/3$, $p = 0.6$, and $p_s = 1.0$ (solid curves). This choice of parameter values corresponds to an average of 2.14 concerted proton jumps per chain.

The differences between the curves in fig. 13 and those for the Markovian case (fig. 12) are due to two opposing factors. First, the directional correlation between successive proton jumps makes charge transport more efficient, which - for given conductivities and given jump frequencies - leads to shorter step lengths $\sigma_{\pm}$ than in the Markovian case. (For $\theta < 90^\circ$, of course, the correlation has the opposite effect.) Second, since all sequential proton jumps are NMR-active, one obtains - for given τ_{exc} - lower jump frequencies, which - for given conductivities and given correlation - leads to longer step lengths $\sigma_{\pm}$ than in the Markovian case. Both these effects are enhanced as the mean chain length $\langle N \rangle$ increases - but at different rates. In the long-chain limit, the geometrical effect

[†] In the planar case, the correlation is due entirely to the impossibility for the charge of retracing any step in a perfectly ($P_R = 0$) concerted transfer chain.

contributes a factor of $(1+\alpha)/(1-\alpha)$ and the frequency effect a factor of 2 to $\sigma_{\pm}^2$. Thus for $\alpha = 1/3$, the two effects cancel exactly in this limit. The geometrical effect obviously increases with increasing θ (cf. curve b in fig. 13).

Compared to the Markovian case (fig. 12), the entire family of curves in fig. 13 is displaced 22 pm towards larger $\sigma_{\pm}$ and are also slightly steeper. For an isotope effect in $\lambda_{\pm}^S$ of 1.19 (corresponding to the experimental results⁸⁹ for Na^+ and K^+), we find $\sigma_+ = 213$ and $\sigma_- = 233$ pm. Considering the experimental uncertainty in our $k_{\pm}$ data, we can not - as in the Markovian case - claim that the resulting $\sigma_{\pm}$ values are inconsistent with the quantum-mechanical oxygen-oxygen distances (sect. 4.3). We must emphasize, however, that the curves in fig. 13 are not to be taken absolutely quantitatively - we have introduced a number of simplifications along the way. Thus one might like to explore the consequences of relaxing the assumption of perfectly ($P_R = 0$) concerted proton jumps and allowing for a finite lifetime of the charge at sequential sites. Furthermore, the re-encounter problem for concerted transfer should be treated in more detail. On the other hand, we do believe that the calculations presented in this section demonstrate certain relevant features of the proton transfer process and that they indicate the possibility of arriving at a consistent picture by allowing for some concertedness in the transfer mechanism.

4.5. TEMPERATURE DEPENDENCE

IG. 14

In fig. 14 we have plotted experimental data, taken from the literature^{4,46,95-98}, for the prototropic conductivities $\lambda_{\pm}$ versus inverse temperature. The quantities $\lambda_{\pm}$ are defined, as in the original work, according to eqn (26) with $\lambda_+^S = \lambda(\text{Na}^+)$ and $\lambda_-^S = \lambda(\text{Cl}^-)$. Since the data refer to saturation conditions, the density varies along the curves. The temperature dependence at constant density⁹⁹ differs from that shown in fig. 14 by less than 5 % up to 100°C, but the sharp decline of $\lambda_{\pm}$ at the highest temperatures is due mainly to the

decrease in density as the critical point is approached. However, the maximum shows up - although less pronounced - also in the constant-density curves⁹⁹.

It is well-known that transport processes in liquid water, e.g. viscosity⁹⁰, reorientation²⁰, water self-diffusion⁹¹, and (non-prototropic) ionic conductivities⁴⁶, cannot be described by Arrhenius' equation over any appreciable temperature range. In the case of the prototropic conductivities $\lambda_{\pm}$, however, the deviation from Arrhenius-behaviour is exceptionally large. We shall now investigate whether this observation can be rationalized in terms of any of the proton transfer models described in sect. 3.

In the Markovian model (sect. 3.2), the rate-determining step consists of collective H-bond reorganizations (bending and stretching). A detailed treatment of these degrees of freedom would pose formidable problems and we shall simply describe them by temperature-independent enthalpies of activation, $\Delta H_{\pm}^{\ddagger}$. In this approximation, the Markovian model thus cannot explain the observed temperature dependence of $\lambda_{\pm}$. In the concerted case (sect. 3.3), however, a temperature dependence enters also via the H-bond probability $p(T)$, which determines (together with p_s) the mean length of proton transfer chains. If $\Delta H_{\pm}^{\ddagger}$ is the activation enthalpy for $\tau_{\pm}$, we obtain from eqn (27), (32), (34), and (35)

$$\ln \lambda_{\pm} = C_{\pm} - \frac{\Delta H_{\pm}^{\ddagger}}{RT} + \ln \left[\sum_{N=2}^{\infty} P(N)(N-1) \left\{ \frac{1+\alpha}{1-\alpha} - \left(\frac{2\alpha}{N-1} \right) \frac{1-\alpha^{N-1}}{(1-\alpha)^2} \right\} \right], \quad (36)$$

where the constants $C_{\pm}$ are assumed to be independent of temperature. The chain length probability $P(N)$ is determined by the H-bond probability p and by the sink-termination probability p_s according to eqn (A4) [with $P(1) = 0$] and (A10) - modified to include polarity correlation.

The H-bond probability p has been determined^{66,67} from vibrational spectra as a function of temperature. The upper curve in fig. 15, which

- like the data in fig. 14 - refers to saturation conditions, has been taken from the work of Luck and coworkers⁶⁶. It should be noted, however, that the procedure employed for extracting p from vibrational spectra has been severely criticized¹⁰⁰. Moreover, it is not at all obvious that a "spectroscopic H-bond" is equivalent to a "proton-transfer H-bond". To participate in a proton transfer chain, a H-bond probably must satisfy comparatively stringent geometrical criteria. Consequently, $P(N)$ should be calculated from lower p values than those given by the upper curve in fig. 15. In view of this difficulty, we shall follow the reverse procedure, i.e., to calculate $p(T)$ from eqn (36) and the experimental data in fig. 14.

To reproduce the observed decrease in the apparent Arrhenius activation enthalpy with rising temperature (fig. 14), we must clearly choose a value of p_s such that the last term in eqn (36) increases with increasing p (decreasing temperature) in the relevant p -range. Essentially, this means that we are confined to curve segments with positive slope in fig. 9.

We shall carry out the calculation for the H_3O^+ data in fig. 14, using[†] $\Delta H_+^\ddagger = 10 \text{ kJ mol}^{-1}$ and $\alpha = 1/3$. Both of these quantities, as well as p_s , are assumed to give rise to a temperature dependence in

[†] This value corresponds to the activation enthalpy $\Delta H^\ddagger(k_+)$ derived⁵¹ from NMR data. According to eqn (31),

$$\Delta H_+^\ddagger = \Delta H^\ddagger(k_+) - RT^2 \frac{d}{dT} \left[\ln \left(\langle N \rangle - \frac{4}{3} \right) \right],$$

i.e., $\Delta H^\ddagger(k_+)$ provides only a lower limit to the activation enthalpy $\Delta H_+^\ddagger$ for τ_+ . However, using data from fig. 9 and 15, we find that the last term is small (ca. 2 kJ mol^{-1}). This correction would lower the curves in fig. 15 by about 0.1 unit.

λ_+ which is negligible compared to that from $p(T)$. The constant C_+ in eqn (36) is fixed by choosing a reasonable value for $p(273K)$. (This value must correspond to a positive slope in fig. 9.)

The general appearance of the four lower curves in fig. 15, i.e., the monotonous reduction of the H-bond probability p with increasing temperature, demonstrate that the concerted proton transfer model is consistent - for a range of values of p_s and $p(273)$ - with the observed anomalous temperature dependence of λ_+^+ . In the case of exclusively dead-end terminated chains ($p_s = 0$), we must have $p(273) \lesssim 0.6$ in order to obtain $dp/dT < 0$. (This is a consequence of the dramatic increase in slope for $p > 0.6$ in fig. 9.) For $p_s = 0$ and $p(273) = 0.6$, the transfer chains involve ca. 10 H-bonds at the lower temperatures, which would lead to inconsistencies in the $\sigma_+ - \lambda_+^S$ plot (sect. 4.4). In the other three cases, however, the mean chain length does not exceed 3.5 H-bonds.

[†] Note that the probability p refers to all H-bonds except the three primary ones in $H_3O^+(H_2O)_3$ and $OH^-(H_2O)_3$, which remain intact even at the highest temperatures considered. [This restriction was formally introduced in appendix A by stipulating that $P(1) = 0$.] Thus $p = 0$ does not imply that $\lambda_{\pm} = 0$, but only that no concerted processes can take place.

4.6. PRESSURE DEPENDENCE

At low ($\lesssim 40^{\circ}\text{C}$) temperatures and low ($\lesssim 100\text{ MPa}$) pressures one finds a complex pressure dependence of transport processes in liquid water. Outside this range, however, the kinetics is slowed down by increasing pressure - just like in "simple" liquids. Thus the viscosity¹⁰¹ goes up, while the water self-diffusion coefficient⁹¹ and (non-prototropic) ionic conductivities¹⁰² are reduced. The prototropic conductivities $\lambda_{\pm}$, however, increase with rising pressure (and density)^{99,103}.

From the data of Franck and coworkers⁹⁹, we may calculate the apparent activation volume $\Delta V_{+}^{\ddagger}$, defined by[†]

$$\Delta V_{+}^{\ddagger} = - RT \left(\frac{\partial \ln \lambda_{+}}{\partial P} \right)_T. \quad (37)$$

It is found that $\Delta V_{+}^{\ddagger}$ is relatively insensitive to temperature but varies markedly with pressure. Thus in the range 0.1 - 100 MPa $\Delta V_{+}^{\ddagger} \approx - 2.5 \pm 1\text{ cm}^3\text{ mol}^{-1}$, while in the range 600 - 800 MPa $\Delta V_{+}^{\ddagger} \approx - 0.4 \pm 0.1\text{ cm}^3\text{ mol}^{-1}$ (K^{+} was taken as the reference ion).

[†] It has been argued¹⁰⁴ that $\Delta V_{+}^{\ddagger}$ in eqn (37) should be replaced by $\Delta V_{+}^{\ddagger} + \frac{2}{3} RT \kappa$, where κ is the isothermal compressibility. The additional term results from the assumption that the rms proton jump distance σ_{+} is proportional to $V^{1/3}$, where V is the solution volume. This assumption is not valid. Indeed, recent computer simulations¹⁰⁵ have shown that the H-bond compression - as reflected in the position of the first maximum of the oxygen-oxygen pair distribution function - is an order of magnitude less than that expected on the basis of a uniform scaling with density of the structure.

The negative sign of the activation volume is consistent with the view (sect. 3.2 and fig. 7) of the activation step as a collective H-bond reorganization leading from a H_3O^+ ion (3 short H-bonds) to a transient H_5O_2^+ configuration (5 short H-bonds). The fact that $\Delta V_{\ddagger}^{\pm}$ becomes less negative with increasing density can be explained along similar lines as the non-Arrhenius temperature dependence. Thus the pressure-induced bending of H-bonds¹⁰⁵ should lower the probability p for "proton-jumpable" H-bonds, which means that any contribution to $\lambda_{\pm}$ from concerted processes should diminish with increasing pressure. [Concerted processes are taken into account formally by adding, to the left-hand side of eqn (37), $-RT$ times the pressure derivative of the last term in eqn (36).]

4.7. ISOTOPE EFFECT

All rate processes in liquid water are slowed down in going from H_2O to D_2O . At 25°C there is a ca. 20 % isotope effect on viscosity⁹⁰ and water self-diffusion¹⁰⁶, while for molecular reorientation¹⁰⁷ the effect is ca. 30 %. These kinetic isotope effects are thought to have their origin in a subtle interplay of vibrational and librational quantum effects, resulting in a net stabilization of the $\text{O}-\text{D}\cdots\text{O}$ bond compared to the $\text{O}-\text{H}\cdots\text{O}$ bond^{7,108}.

The prototropic conductivities $\lambda_{\pm}$ are anomalous also with respect to the isotope effect. Using data from fig. 14, we have in fig. 16 plotted the isotopic ratios $\lambda_{+}^{\text{H}}/\lambda_{+}^{\text{D}}$ and $\lambda_{-}^{\text{H}}/\lambda_{-}^{\text{D}}$ versus temperature in the range $0-100^\circ\text{C}$. Within this range, the variation with temperature is merely ca. 10 % but the magnitudes $\lambda_{+}^{\text{H}}/\lambda_{+}^{\text{D}} = 1.45 \pm 0.05$ and $\lambda_{-}^{\text{H}}/\lambda_{-}^{\text{D}} = 2.1 \pm 0.1$ - are much larger than for other dynamic properties. (As indicated in fig. 16, the ratio $\lambda_{-}^{\text{H}}/\lambda_{-}^{\text{D}}$ is sensitive to the choice of reference ion for λ_{-}^{S} .)

FIG. 16

The isotope effect has been used as a test of various models for prototropic charge transport^{4,5,64,109}. On the basis of the identification $\lambda_+^H/\lambda_+^D \approx 2^{\frac{1}{2}} = (m_D/m_H)^{\frac{1}{2}}$, the isotope effect has thus been ascribed to field-assisted water reorientation⁵ or to stretching vibrations^{64,109}. We feel, however, that such arguments carry very little weight unless also the much larger λ_-^H/λ_-^D ratio can be explained.

In searching for the origin of the isotope effect, and in particular, its larger magnitude for negative charge transport, we must first understand the asymmetry between positive and negative prototropic charge transport. As seen from the upper curve in fig. 16, the ratio λ_+^H/λ_-^H is ca. 2 at high temperatures (at 200°C and $\rho = 0.86 \text{ g cm}^{-3}$ it is 1.74) and probably reaches 3 in the supercooled region. For the deuterated species the ratio λ_+^D/λ_-^D is even larger, ranging from 3.21 at 90°C to 4.10 at 5°C.

It is important to realize that the symmetry between positive and negative prototropic charge transport is of a topological nature (the proton jumps "forwards" or "backwards") and that it does not apply to the energetics of the process. Thus the quantum-mechanical calculations of Newton and Ehrenson⁹ show that the binding energies $E(\text{H}_5\text{O}_2^+) - E(\text{H}_3\text{O}^+) - E(\text{H}_2\text{O})$, $E[(\text{H}_5\text{O}_2^+)\text{H}_2\text{O}] - E(\text{H}_5\text{O}_2^+) - E(\text{H}_2\text{O})$ and $\frac{1}{3} E[\text{H}_3\text{O}(\text{H}_2\text{O})_3] - \frac{1}{3} E(\text{H}_3\text{O}^+) - E(\text{H}_2\text{O})$ are more negative than those for the analogous anionic species by 10 - 30 kJ mol⁻¹. Since the observed activation energies⁵¹ for positive and negative charge transport are nearly the same, these differences in binding energies must cancel in the energy difference between the two nonequivalent configurations schematically illustrated in fig. 7. However, compared to a proton defect, an excess proton must be surrounded by more and stronger H-bonds. As a consequence, concerted processes should be more important, i.e., involve longer chains, for positive charge transport.

Considering the large number of degrees of freedom involved in the activation process (fig. 7) and the likely involvement of concerted processes, we must probably accept that a prediction - from first principles - of the isotope effect on $\lambda_{\pm}$ is beyond reach at present. That a delicate balance of several opposing factors is indeed involved is indicated by the fact that an isotope effect of 1.44 could be caused by a difference in (apparent) activation energies of merely 0.9 kJ mol^{-1} . This figure may be compared to the difference in vibrational (H-bonded O-H stretch) zero-point energy between H_2O and D_2O which amounts to 5.4 kJ mol^{-1} . In addition, there may also be an isotope effect connected with the "pre-exponential factor". (Unfortunately, the accuracy of the data in fig. 14 does not allow us to isolate the contribution to the isotope effect from the apparent activation enthalpy.)

In fig. 16 we have also included the corresponding ratios of rate constants $k_{\pm}$ derived from our NMR measurements (table 3). These ratios are all slightly larger than the corresponding conductivity ratios - if K^+ and F^- are taken as reference ions (sect. 4.3). If - as suggested by the analysis in sect. 4.4 - the Stokesian contributions $\lambda_{\pm}^{\text{S}}$ exceed the conductivities of these reference ions, then the isotope effects deduced from NMR and conductivity would agree more closely.

4.8. SALT EFFECT

For obvious reasons, the salt effect on the limiting prototropic conductivities $\lambda_{\pm}$ cannot be determined with any accuracy. However, the limiting prototropic tracer-diffusion coefficients $D_{\pm}$ in the presence of supporting electrolyte may be obtained from polarography¹¹⁰ or with the diaphragm cell technique⁴⁶. [At finite electrolyte concentrations, $\lambda_{\pm}$ and $D_{\pm}$ are not simply related⁴⁶ - the Nernst eqn (27) is valid only at infinite dilution.] Experimentally it is found^{46,110} that added salt

reduces ionic tracer-diffusion coefficients - more so for H_3O^+ than for, e.g., Na^+ or Cl^- . From the data of Roberts and Northey¹¹⁰ one finds, at 0.15 M KCl, a reduction of D_+ (Cl^- as reference ion) by 10 % in H_2O and by 20 % in D_2O . The NMR data on the salt effect on k_+ (table 3) agree, within the experimental uncertainty, with these figures. Since tracer-diffusion data for OH^- have not been reported, we cannot confirm the reversed isotope effect on the salt effect on k_- (table 3).

In the limit of low salt concentration, the reduction of ionic tracer-diffusion coefficients is usually ascribed to the relaxation of the distorted ionic atmosphere surrounding the diffusing ion⁴⁶. According to a limiting law due to Onsager¹¹¹, the retardation of tracer-diffusion should be most pronounced for highly mobile ions. Although this agrees qualitatively with experiment, the quantitative predictions of the limiting law are in error by a factor of two at a concentration of 0.15 M. Unfortunately, the dynamic theory of electrolyte solutions is, at present, not capable of furnishing higher-order correction terms. At still higher concentrations, where the effect depends strongly on the nature of the salt, the structure-breaking ability of various electrolytes¹¹² as well as polarization effects on the proton transfer potential¹¹⁰ have been invoked to explain the reduced efficiency of prototropic charge transport.

5. SUMMARY

Nuclear magnetic resonance - oxygen-17 scalar relaxation in particular - provides the most direct means of experimentally studying the rate of proton transfer in liquid water. We have presented new NMR data - from H_2O as well as from D_2O - which yield proton transfer rate constants of improved accuracy. The analysis leading to these rate constants differs from previous work in that we recognize the symmetry between hydrated H_3O^+ and OH^- ions (resulting in a different k_- , by a factor of 3/2, compared to previous results) and in that we use a value (81 Hz) for the ^1H - ^{17}O spin-spin coupling constant - strongly suggested by the available experimental data - which is lower than that used in earlier work. NMR-inactive proton transfers were discussed and the associated re-encounter problem treated in some detail. As a result, the previously used relation between the experimental rate constants and the actual proton jump frequencies was revised.

We introduced the concept of the elementary return probability, on the basis of which three limiting models for prototropic charge transport could be formulated: fluctuation transfer, Markovian transfer, and concerted transfer. Fluctuation transfer was discarded - even as a feature superposed on a mechanism capable of producing net charge transport. Furthermore, we argued that water reorientation cannot be involved in the mechanism, since any acceleration of the (too slow) thermal reorientation would require high-energy configurations which are inconsistent with the low activation energy for proton transfer. The isotope effect cannot be used as an argument in favour of field-induced water rotation as the rate-limiting step, since it far exceeds $\sqrt{2}$ for negative charge transport. Rather, we believe that the rate-limiting step consists of a collective H-bond reorganization - involving stretching and bending, but no breaking of H-bonds. This picture is consistent with the negative activation volume for proton transfer.

A comparison of NMR and conductivity data disclosed that a strictly Markovian (single-step) model leads to elementary step lengths that are shorter than the minimum oxygen-oxygen separation

in H_5O_2^+ or H_3O_2^- , as predicted by accurate quantum-mechanical calculations. It was shown - in a semi-quantitative way - that this inconsistency can be removed by allowing for some concertedness in the proton transfer process. The conclusion that proton transfer occurs through concerted chains (involving a few H-bonds) was corroborated by the finding that this mechanism - in conjunction with a H-bond probability which decreases monotonically with rising temperature - can account for the anomalous temperature dependence of the prototropic conductivities. Concerted proton transfer should become less important at higher density because of H-bond bending, which explains the anomalous pressure dependence. The considerably higher efficiency of positive (as opposed to negative) prototropic charge transport may be a consequence of the more extensive H-bonding around a H_3O^+ ion (compared to OH^-), which should favour concerted multi-step processes.

The analysis indicated that also the normal (Stokesian) contribution to prototropic charge transport is anomalous in the sense that (1) it is higher than that of non-prototropic ions with similar crystal radii, and/or (2) it is independent of the isotope effect on viscosity. We regard the former alternative as the more likely one (see below).

A topological model describing proton transfer chains in water was formulated. According to this model, transfer chains are unlikely to extend over more than a few H-bonds (at any temperature). This prediction was confirmed by the experimental data. The extension of proton transfer chains is not limited by a lack of H-bonds, but rather by the abundance of H-bonds (at normal temperatures). The chains are thus thought to be terminated mainly at energetic sinks, i.e., the charge migrates preferentially to prehydrated sites with an optimal H-bond configuration.

On account of the high mobility of prototropic charges - the mean residence time per site is 1.3-2 ps for positive charges in H_2O - there is not enough time to establish a long-range orientational

polarization of the medium. Consequently, prototropic ions should experience little dielectric friction, which explains the high Stokesian mobilities that emerged from our analysis. The absence of long-range perturbation of the water structure may also explain why H_3O^+ as counterion does not give rise to a repulsive hydration force between mica surfaces.

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APPENDIX A. TOPOLOGY OF PROTON TRANSFER CHAINS IN LIQUID WATER

In this appendix we use topological arguments to estimate the length distribution for H-bonded chains which can serve as pathways for concerted proton transfer in liquid water. First we consider chains in pure water and then the treatment is extended to take into account the presence of prototropic ions as well as correlation effects and different modes of chain termination.

The physical system is represented by a model, defined by the following four postulates.

- (I) The system is topologically equivalent to a collection of sites (oxygen atoms) residing in a topological space of infinite extent.
- (II) The sites are tetravalent, i.e. any site can be connected to n other sites via n (hydrogen) bonds, with $0 \leq n \leq 4$. Thus only "single bonds" are permitted.
- (III) The bonds have polarity; a site can act either as a donor or as an acceptor of a given bond.
- (IV) A given site can have no more than two bonds of the same polarity.

We begin with the simplest case where the bonds are completely uncorrelated. Hence we introduce the additional two postulates.

- (V) There is no bond correlation, i.e., the bond probability p is independent of the bonding status (the number of bonds and their polarity) of the site.

(VI) There is no polarity correlation, i.e., apart from the constraint (IV), the bond polarity distribution at a given site is random and independent of the bonding status of the site.

The bond probability p is the only parameter in the completely uncorrelated version of the model. Its value is influenced by changes in temperature, density, isotopic composition, etc.

Let $f(n)$ be the probability that a randomly selected site is an n -site, i.e., that it has n bonds (of unspecified polarity). From postulates (II) and (IV) it follows that $f(n)$ is given by the binomial distribution as

$$f(n) = \binom{4}{n} p^n (1-p)^{4-n} . \quad (A1)$$

Consequently

$$p = \frac{\langle n \rangle}{4} , \quad (A2)$$

where $\langle n \rangle \equiv \sum_n n f(n)$ is the mean number of bonds per site. Equation (A1) is in perfect accord with results from computer simulations^{60,61}, thus corroborating postulate (II). Postulate (V), however cannot be tested in this way since the simulations are based on the approximation of pairwise additivity for the intermolecular potentials.

The sites may be divided into two disjoint classes: terminal sites (T-sites), which have bonds of only one polarity, and sequential sites (S-sites), which have at least one bond of each polarity. From postulates (II) and (IV) it follows that $0 \leq n_T \leq 2$ and that $2 \leq n_S \leq 4$. The chain direction is (arbitrarily) defined as that in which a positive prototropic charge would propagate. The T-sites may then be further divided into two subclasses (not disjoint): initial sites (T_i -sites), which have no acceptor bond, and final sites (T_f -sites), which have no donor bond. It will prove

convenient to distinguish also acceptor sites (A-sites), which have at least one acceptor bond. Clearly, all S-sites are also A-sites. The converse is not true, however, since an A-site may be a T_f -site. Furthermore, the class of A-sites and the class of T_i -sites are disjoint and exhaustive.

A chain of N sites is a directed pathway which starts on a T_i -site, traverses $N-2$ S-sites, and ends on a T_f -site. (In the trivial case $N = 1$, the T_i -site and the T_f -site are identical.) A chain, as here defined, is an object in topological space rather than a sequence of sites in physical space. While always being open-ended, a topological chain may cross itself (at 4-sites) and may form closed loops (containing at least three sites). Moreover, a given loop may be traversed any number of times within the same chain. (In physical space, a given bond can never participate more than once in the same concerted chain since proton transfer leads to reversal of polarity.) However, loops will contribute significantly to the chain length distribution only for rather large N . Since only short chains will be of interest, we may therefore disregard the distinction between physical and topological chains.

Let $P(N)$ be the probability that a randomly selected chain traverses precisely N sites. Since this probability refers to disjoint elementary events in an enumerably infinite sample space, we have

$$\sum_{N=1}^{\infty} P(N) = 1. \quad (A3)$$

Since, by definition, a chain contains one T_i -site and one T_f -site with unit probability, we find for $N \geq 2$

$$P(N) = [1-P(1)][1-P_f]^{N-2}P_f, \quad (A4)$$

where P_f is the probability that an A-site is a T_f -site and where $P(1)$ is simply the probability that a T_i -site is a 0-site.

Let $\langle N \rangle$ be the mean number of sites traversed in a chain, i.e.,

$$\langle N \rangle = \sum_{N=1}^{\infty} N P(N). \quad (A5)$$

This quantity will be referred to, somewhat loosely, as the mean chain length. After substitution of $P(N)$ from eqn (A4) we can sum the geometric series to obtain

$$\langle N \rangle = \frac{1}{P_f} \left[\frac{1-P_f^2}{1-P_f} - P(1) \right]. \quad (A6)$$

It remains now only to express P_f and $P(1)$ in terms of the probabilities $f(n)$ given by eqn (A1). Straightforward probability considerations lead to

$$P_f = \frac{f(1)/2 + f(2)/4}{1-f(0)-f(1)/2-f(2)/4} = \frac{p(2-p/2)(1-p)^2}{1-(1+p^2/2)(1-p)^2}, \quad (A7)$$

$$P(1) = \frac{f(0)}{f(0)+f(1)/2+f(2)/4} = \frac{(1-p)^2}{1+p^2/2}. \quad (A8)$$

Upon substitution of these expressions into eqn (A6) we obtain the remarkably simple result

$$\langle N \rangle = [(1+p^2/2)(1-p)^2]^{-1}. \quad (A9)$$

We must now consider in what respects the preceding treatment should be modified when we stipulate that a chain always starts at a prototropic ion, say H_3O^+ . As a first approximation, we may simply set $P(1) = 0$, since, at any reasonable temperature, the H_3O^+ ion donates at least one H-bond. Neglecting effects of any further influence of the H_3O^+ ion on the water structure, we then obtain, from eqn (A6) and (A7), an expression for $\langle N \rangle$ as a function of p . This result is shown in fig. 9 (dashed curve labeled $p_s = 0$) [Eqn (A9) yields a closely similar curve;

it starts at $\langle N \rangle = 1$ (rather than 2) and ends ($p = 1$) $4/9$ unit below the depicted curve.]

It is also of interest to investigate the effect of relaxing postulate (VI), i.e., of allowing for polarity correlation. This can be done simply by postulating that all 2-sites be S-sites. The sole effect of this constraint is the disappearance of the term $f(2)/4$ from the numerator of eqn (A7). The resulting expression [with $P(1) = 0$] for $\langle N \rangle$ is plotted in fig. 9 (solid curve labeled $p_s = 0$). As expected, the mean chain length increases relative to the uncorrelated case.

Hitherto, we have assumed that a chain ends at the first site encountered with no donor bond. Such chains may be called dead-end chains. It is also conceivable that a chain ends at a sufficiently energetically favourable site. We will refer to such chains as sink-terminated. The natural definition of a sink is an A-site with two donor bonds. Such a site will, upon arrival of the positive charge, constitute a triply donating $H_3O^+(H_2O)_3$. To take into account that a chain now may be terminated either at a sink or at a dead-end, we must replace P_f of eqn (A7) by

$$P_f = \frac{f(1)/2 + f(2)/4 + p_s[f(3)/2 + f(4)]}{1 - f(0) - f(1)/2 - f(2)/4}, \quad (A10)$$

where p_s is the sink-termination probability. For $p_s = 0$ we recover the dead-end result (A7), while for non-zero p_s there is a finite probability for chain termination at a sink site encountered before a dead-end. As before, polarity correlation can be introduced simply by omitting the term $f(2)/4$ in the numerator of eqn (A10).

The mean chain length $\langle N \rangle$ resulting from the substitution of eqn (A1) and (A10) into eqn (A6) with $[P(1) = 0]$ is shown in fig. 9 for $p_s = 0.1, 0.2, 0.4$, and 1 - in all cases with polarity correlation.

The possibility of sink-termination drastically shortens the chains at high values of p . At low bond probabilities long chains are precluded by the frequent dead-ends, while in the extensively bonded range (high p) the chain length is limited by the high sink density.

APPENDIX B. RE-ENCOUNTER KINETICS AND MARKOVIAN PROTON TRANSFER

Consider the oxygen atom of a given prototropic ion, H_3O^+ or OH^- , in liquid water. In order to describe the transient kinetic behaviour of this particular oxygen atom - prototropic charge pair, we need a microscopic model for the molecular motion. We focus here on Markovian proton transfer, which we model as a random walk on a lattice of oxygen atoms.

Let the original encounter define the origin. Anticipating the results of the calculation, we assume that the overwhelming majority of re-encounters are preceded by only short excursions from the origin. It is then reasonable to model the process as a random walk on a lattice, which has the connectivity of a continuously branching loop-free tree with the local topology of a graphite lattice (upper part of fig. 17). Since the three branches emanating from the origin are equivalent, we may restrict our attention to a single branch by stipulating that the first site (the origin) be perfectly reflecting. The two-dimensional lattice thus reduces to one dimension (lower part of fig. 17) with transition probabilities $p = 2/3$ away from and $q = 1/3$ back towards the origin. At the reflecting site, however, we have $p_{1 \rightarrow 2} = 1$.

In order to make use of the theory of finite Markov chains¹¹³, we let the M :th site be perfectly absorbing, i.e., $q_{M-1 \leftarrow M} = 0$. The limit M can always be chosen large enough that boundary effects become negligible. [This is the case when $M \tau_{\pm}$ is on the order of the dwell time (sect. 4.1).]

Let $P_R(N)$ be the probability of any (not necessarily the first) re-encounter after precisely N steps. Obviously $P_R(N) = 0$ for odd N . [The elementary return probability P_R , introduced in eqn (22), is identical to $P_R(2)$.] It can be shown¹¹³ that

$$P_R(N) = (P_{\equiv}^N)_{11}, \quad (\text{B1})$$

where $\underline{P}$ is the one-step transition probability matrix. From fig. 17 it follows that the nonzero elements of $\underline{P}$ are

$$\begin{aligned} P_{12} &= P_{MM} = 1 \\ P_{k,k-1} &= q, \quad 2 \leq k \leq M-1. \\ P_{k,k+1} &= p \end{aligned} \tag{B2}$$

Let $\gamma(N)$ be the mean number of re-encounters after N steps and $\bar{\gamma} \equiv \gamma(N \rightarrow \infty)$ the mean total number of re-encounters. Clearly

$$\gamma(N) = \sum_{N'=1}^N P_R(N'). \tag{B3}$$

Figure 10 shows $\gamma(N)$, calculated from eqn (B1) - (B3) with $M = 100$, as a function of the number N of steps taken after the original encounter. We see that $\gamma = 1$, i.e., a given oxygen atom will, on the average, encounter a prototropic charge twice before "loosing sight" of it. Moreover, some 80 % of the re-encounters occur within the first ten steps after the original encounter - a fact that supports the validity of our lattice model.

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TABLE 1. DETERMINATIONS OF THE SPIN-SPIN COUPLING CONSTANT IN
H₂O FROM ¹⁷O TRIPLET SPECTRA

Solvent	T/°C	x _w ^a	J _{OH} /Hz	Ref.
CH ₃ COCH ₃	29.8	0.30	82 ± 1	22
CH ₃ COCH ₃	~ 25 ^b	0.11	73.5 ± 2.1 ^c	33
CD ₃ COCD ₃	28.4	0.013	79.6 ± 0.7 ^c	this work ^e
CD ₃ CN	28.4	0.025	81.0 ± 0.3	this work ^e
CD ₃ CN	28.4	0.003	81.2 ± 0.3	this work ^e
CD ₃ CN	63.8	0.003	81.1 ± 0.3	this work ^e
CH ₃ NO ₂	~ 25 ^b	0.03	83.5 ± 1	34
CCl ₄	~ 25 ^b		79.9	35
NH ₃ (l)	29.6	<0.10	80	36
Vapor	175, 215		79 ± 2	37
Mean (± std.dev.)			81.0 ± 1.4 ^d	

^a Mole fraction H₂O.

^b Temperature not reported, 25°C assumed.

^c Too small value due to relaxation - broadened, incompletely resolved triplet.

^d Excluding the two results from incompletely resolved spectra.

^e The solvents were of spectroscopic purity (Ciba-Geigy) and the water (Norsk Hydro) of the following isotopic composition: 21.72 % ¹⁷O, 62.23 % ¹⁸O, 0.014 % ²H. The measurements were made at 34.56 MHz on a home-built Fourier-transform spectrometer using (5-20)·10⁴ transients with pulse repetition times of 50 - 100 ms giving signal-to-noise ratios exceeding 200. The linewidths (including ~6 Hz inhomogeneity broadening) were 60 Hz (CD₃COCD₃), 36 Hz (CD₃CN, 28.4°C), and 30 Hz (CD₃CN, 63.8°C).

TABLE 2. MOLARITY-pH CONVERSION FACTORS.

Sample	T/°C	γ_+^m	pK_w^m	F_w^m	α_+^f	$10^{-14} \alpha_-^f$
H ₂ O	28.4	1	13.894±0.005 ^c	1	1.02	0.80±0.01
0.15 M KCl/H ₂ O	27.0	0.75±0.02 ^a	13.939±0.005 ^c	0.595±0.001 ^e	0.76±0.02	0.70±0.02
D ₂ O	27.7	1	14.863±0.001 ^d	1	2.58±0.18	2.37±0.16
0.15 M KCl/D ₂ O	28.1	0.75±0.02 ^{a,b}	14.849±0.001 ^d	0.595±0.001 ^{e,b}	1.92±0.14	1.81±0.13

^a Calculated from (1) the Debye-Hückel theory⁴³ and from (2) the experimental activity coefficient function⁴⁵ and the water activity⁴⁶.

^b The H/D solvent isot effect has been neglected⁴⁷.

^c Ref. 48.

^d Ref. 49.

^e Ref. 45.

^f Calculated according to eqn (16) - (19).

TABLE 3. RATE CONSTANTS AT 28.0°C FOR PROTOTROPIC CHARGE TRANSFER IN WATER AND AQUEOUS KCl SOLUTIONS AS DERIVED FROM ^{17}O RELAXATION DATA.

Sample	$k_+/10^9 \text{ M}^{-1}\text{s}^{-1}$	$k_-/10^9 \text{ M}^{-1}\text{s}^{-1}$	k_+/k_-
H_2O	7.1 ± 0.4	3.4 ± 0.2	2.1 ± 0.1
0.15 M KCl/ H_2O	7.3 ± 0.5	2.4 ± 0.2	3.0 ± 0.1
D_2O	4.3 ± 0.5	1.2 ± 0.2	3.5 ± 0.2
0.15 M KCl/ D_2O	3.4 ± 0.4	1.4 ± 0.2	2.4 ± 0.3

Sample	$k_+^{\text{H}}/k_+^{\text{D}}$	$k_-^{\text{H}}/k_-^{\text{D}}$
Pure water	1.6 ± 0.2	2.7 ± 0.4
0.15 M KCl	2.2 ± 0.3	1.8 ± 0.3

Sample	k_+^0/k_+^{KCl}	k_-^0/k_-^{KCl}
H_2O	1.0 ± 0.1	1.4 ± 0.1
D_2O	1.3 ± 0.2	0.9 ± 0.2

Experimental details: Doubly distilled (quartz apparatus) H_2O or >99.7% D_2O (Ciba-Geigy) was enriched to ca. 1% ^{17}O by addition of 10% H_2^{17}O or D_2^{17}O (Norsk Hydro). KCl was of Suprapur quality (Merck). pH was adjusted with HCl (DC1) and KOH (KOD) and measured with a Radiometer PHM52 instrument equipped with a GK 2322C glass electrode, which was calibrated in three standard buffers (pH 4.01, 7.00, and 9.18). Reported linewidths (fig. 2-5) are averages of 2-4 spectra recorded at 13.56 MHz or 34.56 MHz (the pure D_2O sample). The probe was thermostated to within $\pm 0.3^\circ\text{C}$. The estimated uncertainty in linewidth is $\pm 0.5 \text{ Hz}$.

and in pH ± 0.05 units. Reported pH values (fig. 2-5) were measured before recording the spectra. The absence of pH drift (no buffer was added) was confirmed by the observation that the linewidth remained constant between several consecutive spectra recorded at each pH. This was the case even in the steep parts of fig. 2-5, where the linewidth is extremely sensitive to pH. The reported uncertainties in $k_{\pm}$ are based on (1) uncertainties in fits estimated visually by independent variations of k_{+} and k_{-} taking into account the experimental uncertainties in linewidths and pH, (2) estimated uncertainties in the spin-spin coupling constants according to $J_{OH}=81.1\pm 1.0$ Hz and $J_{OD}=12.45\pm 0.15$ Hz, and (3) uncertainties in the conversion factors $\alpha_{\pm}$ (table 2). The four sets of data were recorded at slightly different temperatures (table 2). The rate constants were subsequently converted to 28.0°C using activation energies⁵¹ of 10.0 kJ mol⁻¹ (k_{+}) and 8.8 kJ mol⁻¹ (k_{-}). Salt and isotope effects on these activation energies were neglected, however, the corrections amounted to <1.3% (H₂O) and <0.4% (D₂O).

TABLE 4. RATE CONSTANTS AT 28.0°C FOR PROTOTROPIC CHARGE TRANSFER IN H₂O AS DERIVED FROM NMR DATA.

$k_+/10^9 \text{ M}^{-1} \text{ s}^{-1}$	$k_-/10^9 \text{ M}^{-1} \text{ s}^{-1}$	k_+/k_-	Ref.
5.5 ± 2.1	3.0 ± 1.2	1.8 ± 1.0	15
5.8 ± 0.6	4.3 ± 0.8	1.3 ± 0.3	26
	3.3		30
5.5	2.2	2.5	51
	2.7		52
4.1	3.5	1.2	27
4.2	3.6	1.2	22
7.1 ± 0.4	3.4 ± 0.2	2.1 ± 0.1	this work

Previous data, obtained at 25 or 26°C with $J_{\text{OH}}=92.3$ or 97.6 Hz, have been converted to 28.0°C and $J_{\text{OH}}=81.1$ Hz using activation energies⁵¹ of 10.0 kJ mol⁻¹ (k_+), 8.8 kJ mol⁻¹ (k_-) and using eqn (8), respectively. We quote $k_{\pm}$ as defined by eqn (14), whereas previous authors have reported the rate constants $k_1 = \frac{3}{2} k_+$ and $k_2=k_-$ (cf. sect. 4.1).

TABLE 5. MEAN LIFETIMES AT 28.0°C for PROTOTROPIC IONS IN WATER AND AQUEOUS KCl SOLUTIONS AS DERIVED FROM ^{17}O RELAXATION DATA UNDER THE ASSUMPTION OF MARKOVIAN TRANSFER.

Sample	τ_+ /ps	τ_- /ps
H_2O	1.27 ± 0.06	2.6 ± 0.1
0.15 M KCl/ H_2O	1.24 ± 0.09	3.7 ± 0.3
D_2O	2.1 ± 0.3	7.3 ± 0.9
0.15 M KCl/ D_2O	2.7 ± 0.3	6.5 ± 0.8

The lifetimes were calculated by eqn (24) with rate constants from table 3 and with $\gamma=1$. The value $\gamma=1$ is derived in appendix B under the assumption of Markovian proton transfer.

The various ratios of lifetimes are equal, within the given uncertainties, to the inverses of the corresponding ratios of rate constants in table 3.

TABLE 6. MEAN LIFETIMES AT 28.0°C FOR (TERMINAL) PROTOTROPIC IONS IN WATER AS DERIVED FROM ^{17}O RELAXATION DATA UNDER THE ASSUMPTION OF PERFECTLY CONCERTED TRANSFER.

<N>	$\tau_{\pm}/\text{ps}$			
	H_3O^+	OH^-	D_3O^+	OD^-
3	4.2 ± 0.2	8.8 ± 0.5	7.0 ± 0.9	24 ± 3
4	6.8 ± 0.3	14 ± 1	11 ± 1	39 ± 5
5	9.3 ± 0.5	20 ± 1	15 ± 2	54 ± 6

The lifetimes were calculated by eqn (31) with rate constants from table 3.

FIGURE CAPTIONS

- FIG. 1. The ratio of the "exact" exchange time τ_{exc} , as calculated from eqn (8), to the approximate exchange time τ'_{exc} , as calculated from eqn (2), versus $\log \tau_{\text{exc}}$ and the apparent scalar relaxation rate R_S . The continuation of the D_2O curve is shown to the right on a tenfold expanded scale. The calculations are based on $R_Q = 130 \text{ s}^{-1}$, $J_{\text{OH}} = 81.1 \text{ Hz}$ for H_2O and $R_Q = 168 \text{ s}^{-1}$, $J_{\text{OD}} = 12.45 \text{ Hz}$ for D_2O .
- FIG. 2. Oxygen-17 linewidth versus pH in H_2O at 28.4°C . The estimated experimental uncertainty is contained within the circles. The curve resulted from a two-parameter fit according to eqn (8), (14), and (19).
- FIG. 3. Oxygen-17 linewidth versus pH in $0.15 \text{ M KCl}/\text{H}_2\text{O}$ at 27.0°C . The estimated experimental uncertainty is contained within the circles. The curve resulted from a two-parameter fit according to eqn (8), (14), and (19).
- FIG. 4. Oxygen-17 linewidth versus pH_D in D_2O at 27.7°C . The estimated experimental uncertainty is shown on one data point. The curve resulted from a two-parameter fit according to eqn (8), (14), and (19).
- FIG. 5. Oxygen-17 linewidth versus pH_D in $0.15 \text{ M KCl}/\text{D}_2\text{O}$ at 28.1°C . The estimated experimental uncertainty is shown on one data point. The curve resulted from a two-parameter fit according to eqn (8), (14), and (19).
- FIG. 6. Schematic representation of the elementary steps in prototropic charge transport.
- FIG. 7. Schematic representation of prototropic charge transfer with rate-limiting bond-length reorganization.

FIG. 8. Schematic representation of a two-step concerted proton transfer. The intermediate configuration corresponds to the transition state. The second step involves concerted transfer of protons H_1 and H_2 .

FIG. 9. The mean number $\langle N \rangle$ of oxygen atoms in a proton transfer chain versus the H-bond probability p . The curves are based on the topological model in appendix A. Dashed curves without and solid curves with polarity correlation. The sink-termination probability p_s for each curve is indicated.

FIG. 10. The mean number $\gamma(N)$ of re-encounters between an initially separating oxygen - charge pair as a function of the number N of subsequent proton transfer steps. The process is modeled as a random walk on a finite lattice, as described in appendix B.

FIG. 11. The mean water lifetime τ_w at 28°C versus pH (or pH_D for D_2O). The dashed lines represent the given asymptotic expressions for τ_w/s .

FIG. 12. The elementary step length $\sigma_{\pm}$ versus the Stokesian contribution $\lambda_{\pm}^S$ to the conductivity. The curves are based on NMR and conductivity data and on the assumption of Markovian proton transfer. The horizontal lines correspond to $\lambda_{\pm}^S(\text{H}_2\text{O})/\lambda_{\pm}^S(\text{D}_2\text{O}) = \eta(\text{D}_2\text{O})/(\text{H}_2\text{O}) = 1.22$. The hatched areas represent experimental uncertainty.

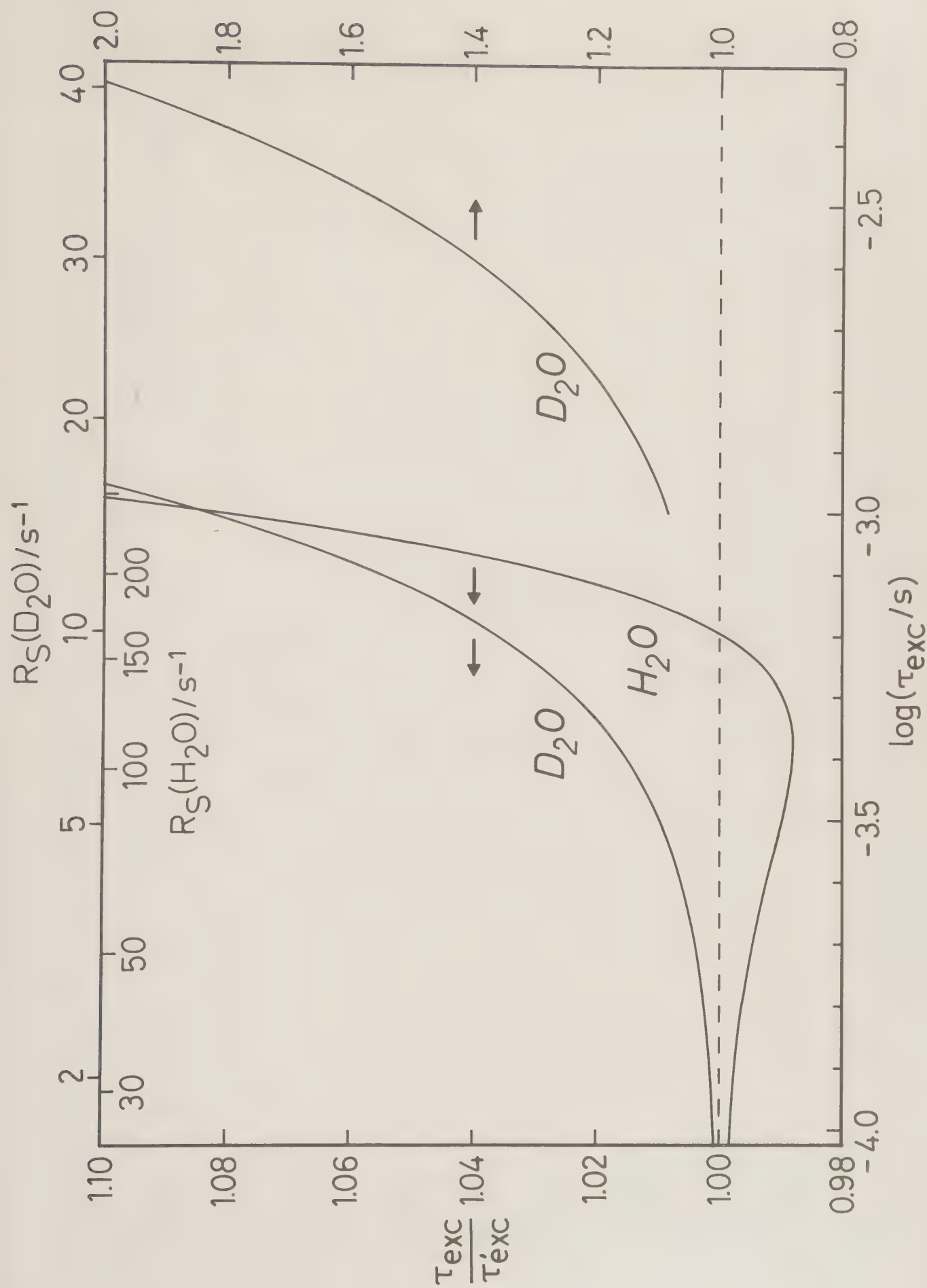
FIG. 13. The elementary step length $\sigma_{\pm}$ versus the Stokesian contribution $\lambda_{\pm}^S$ to the conductivity. The curves are based on NMR and conductivity data and on a model for concerted proton transfer (appendix A). Selected values for the three parameters in the model are given in the insert. (Different combinations of p and p_s corresponding to the same $\langle N \rangle$ yield nearly identical curves.) The horizontal lines correspond to $\lambda_{\pm}^S(\text{H}_2\text{O})/\lambda_{\pm}^S(\text{D}_2\text{O}) = 1.19$ (upper lines) and 1.22 (lower lines).

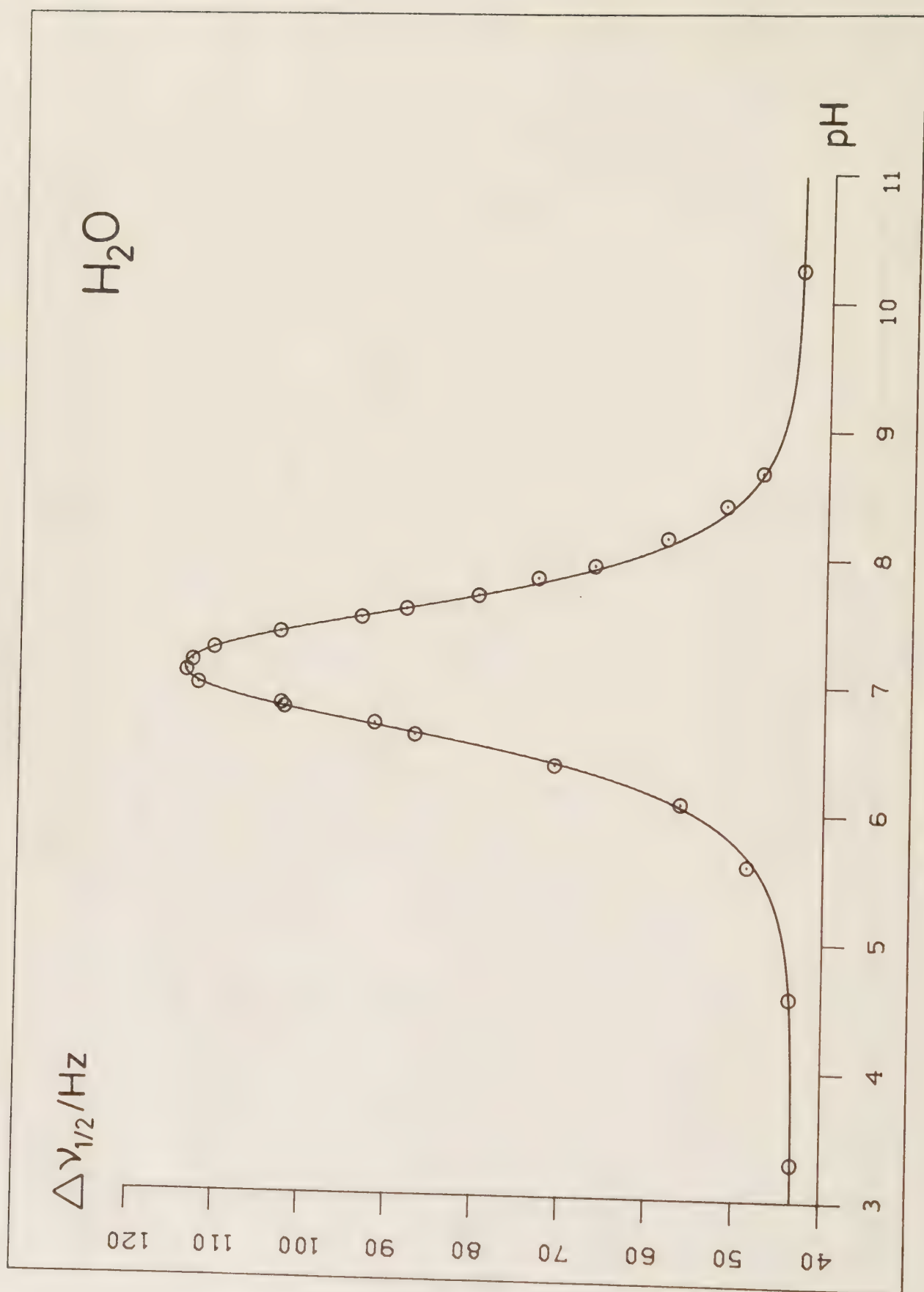
FIG. 14. Arrhenius plot for the prototropic conductivities $\lambda_{\pm}$ (Na^+ and Cl^- as reference ions). The data were taken from ref. 4 (o), 46 ($\blacktriangle$), 95 ($\blacksquare$), 96 ($\blacktriangledown$), 97 ($\triangle$), and 98 ($\bullet$). The curves were drawn merely to facilitate interpolation.

FIG. 15. The H-bond probability p versus temperature as calculated from eqn (36), using $\lambda_+(T)$ data from fig. 14 (H_3O^+) and a temperature-independent activation enthalpy $\Delta H_+^\ddagger = 10 \text{ kJ mol}^{-1}$. Furthermore, we used $\alpha = 1/3$, p_s as indicated beside the curves, and $p(273 \text{ K}) = 0.4, 0.5, \text{ or } 0.6$. The upper (dashed) curve was derived from IR data in ref. 66. All curves refer to saturation conditions.

FIG. 16. Ratios of prototropic conductivities (from fig. 14) - showing the kinetic isotope effect and the asymmetry between positive and negative charge transport - versus temperature. Also shown are the corresponding ratios of conductivities with K^+ and F^- as reference ions, at 25°C ($\bullet$), and of rate constants (table 3), at 28°C (o).

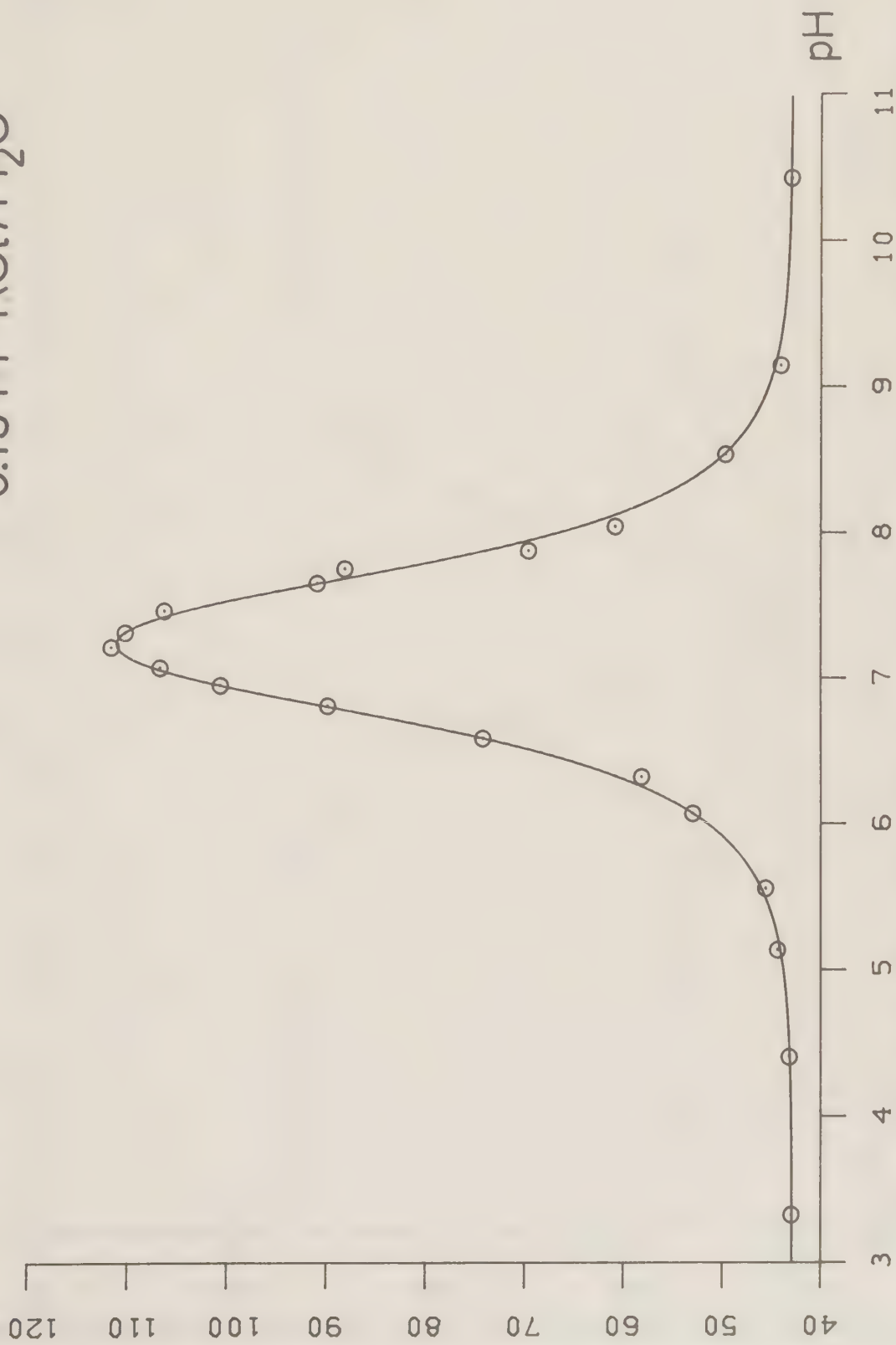
FIG. 17. Modeling Markovian charge transfer as a one-dimensional random walk between a reflecting (1) and an absorbing (M) site.

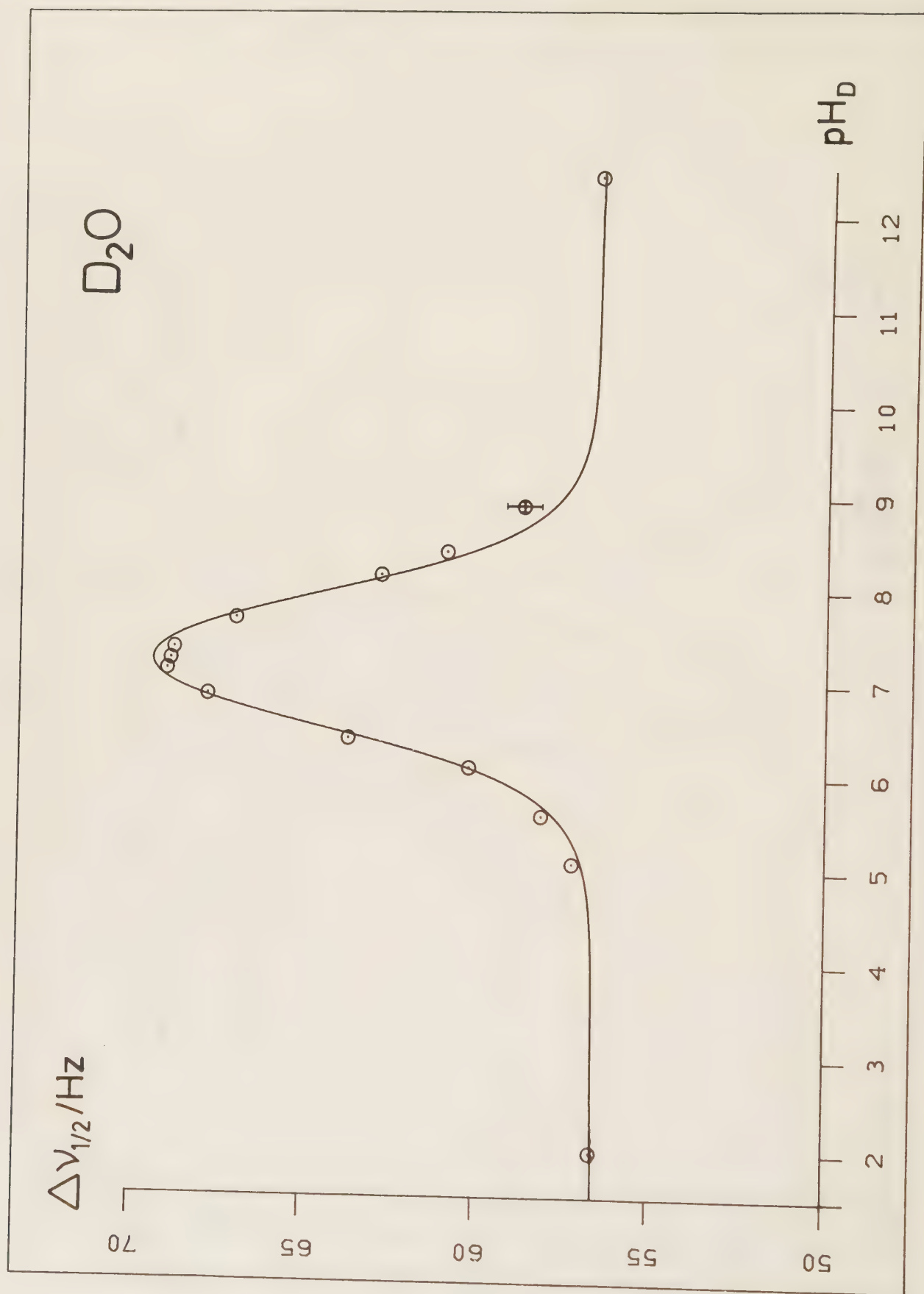


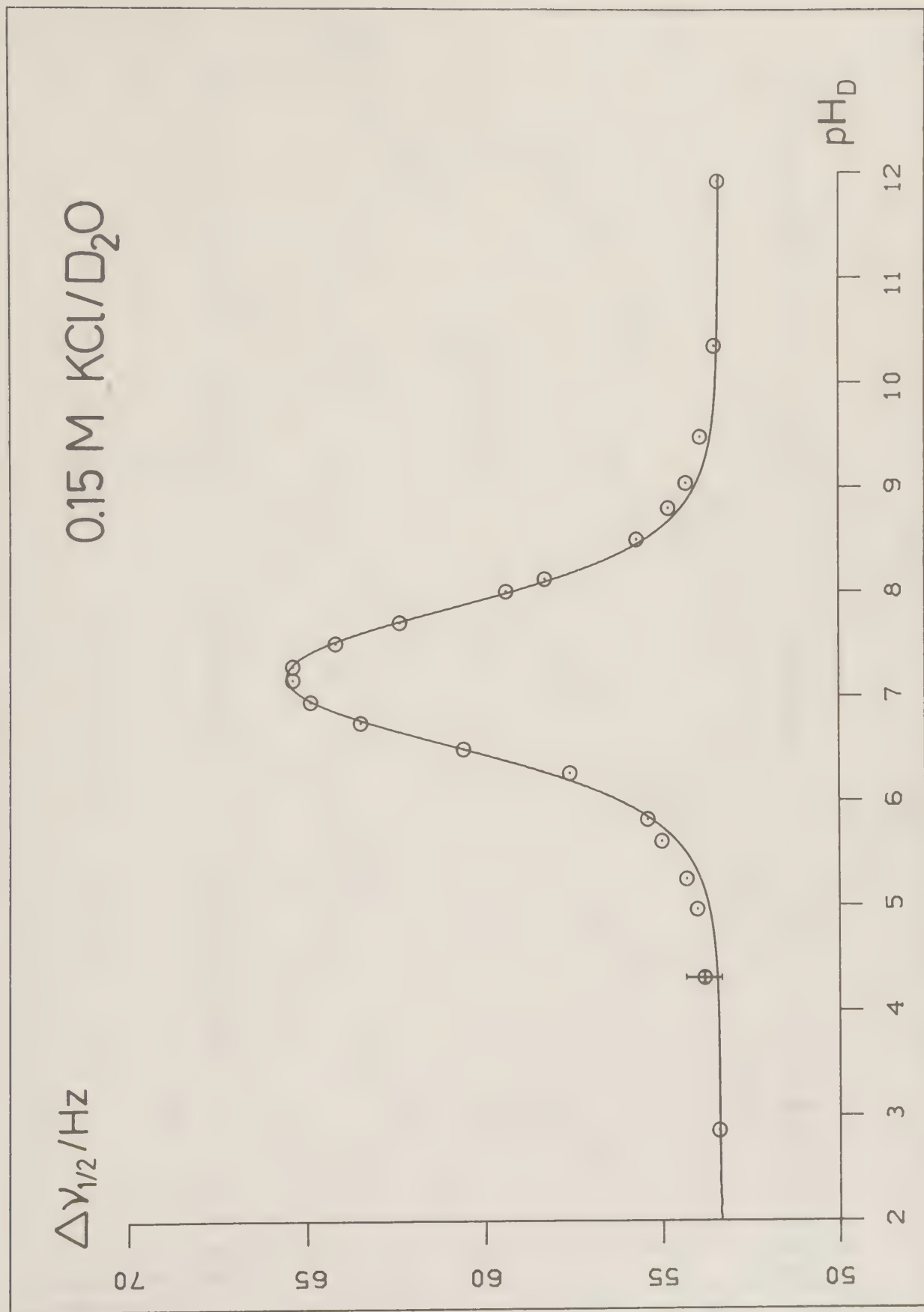


$\Delta\nu_{1/2}/\text{Hz}$

0.15 M KCl/H₂O









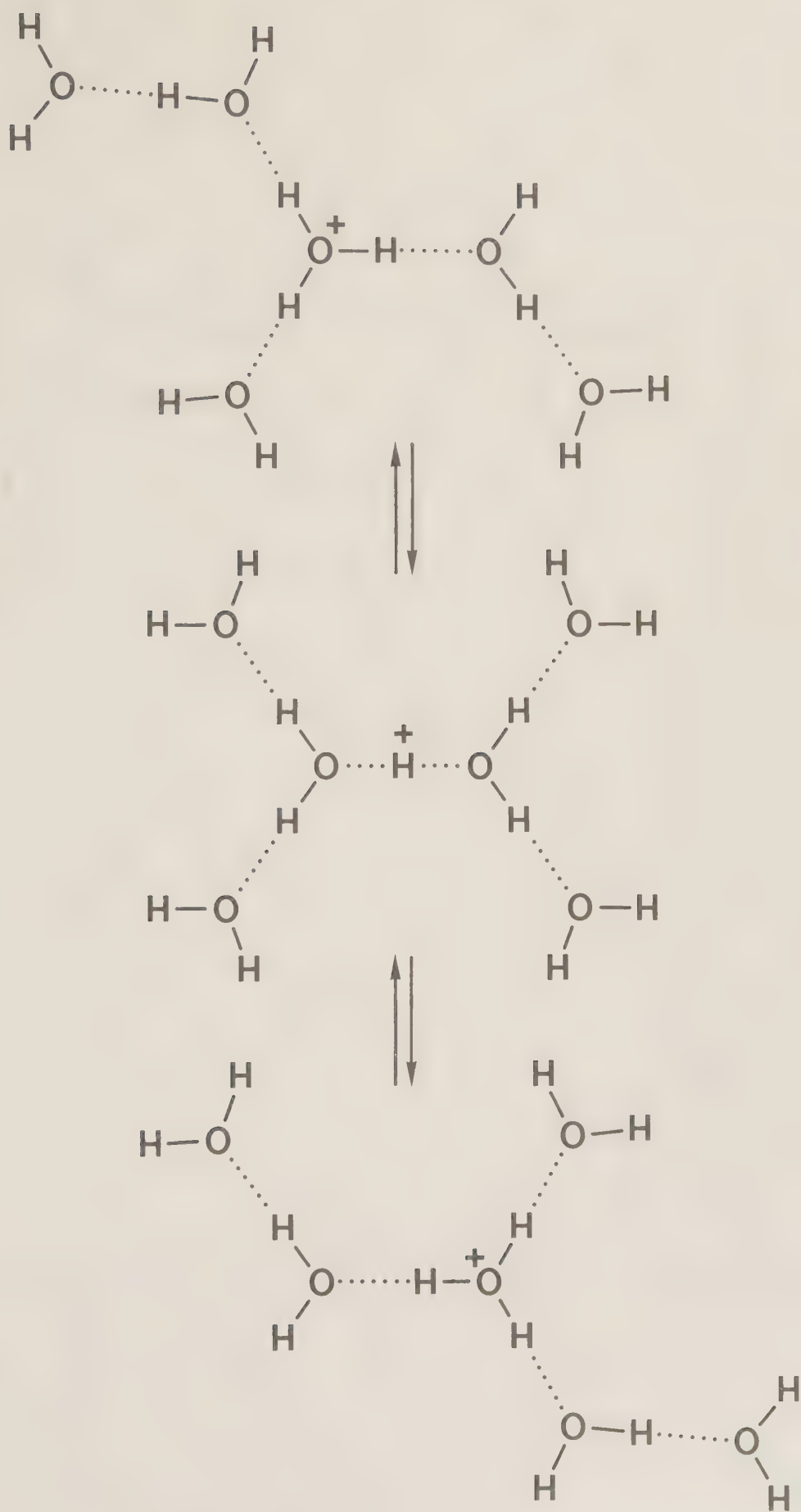


FIG. 7

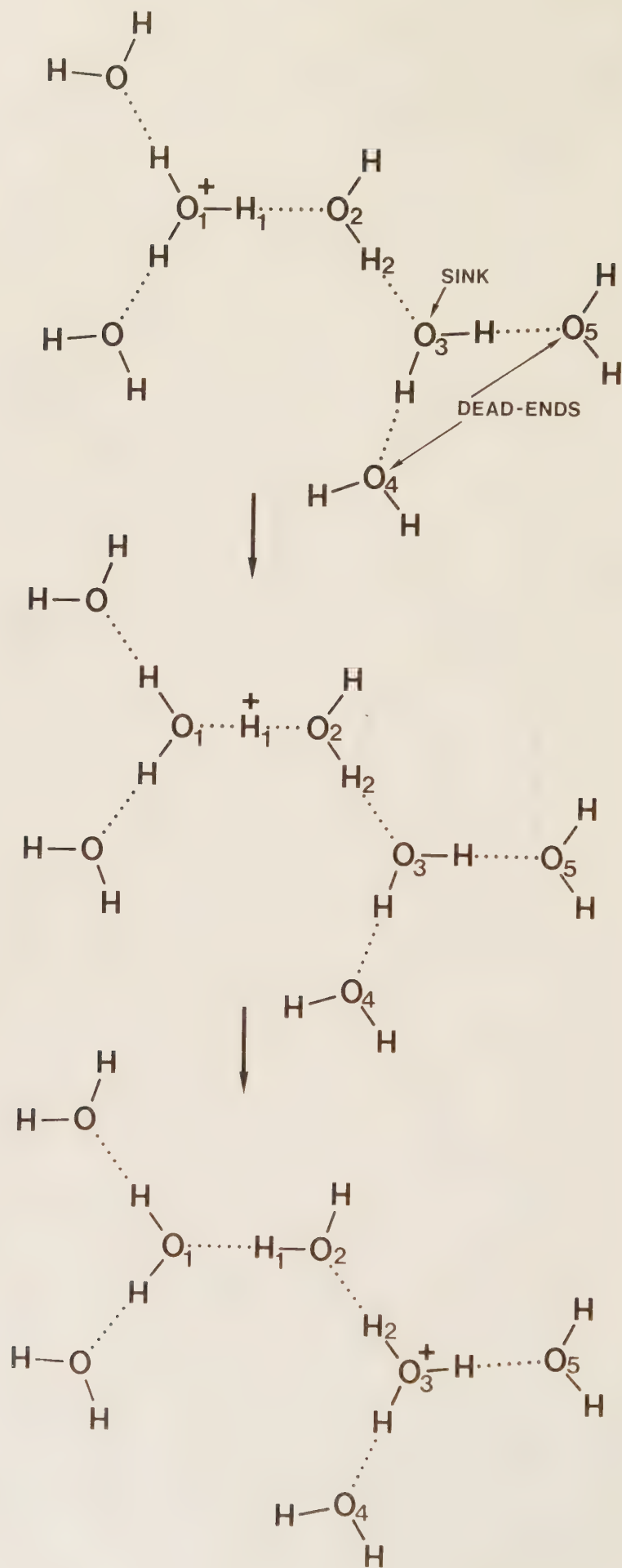
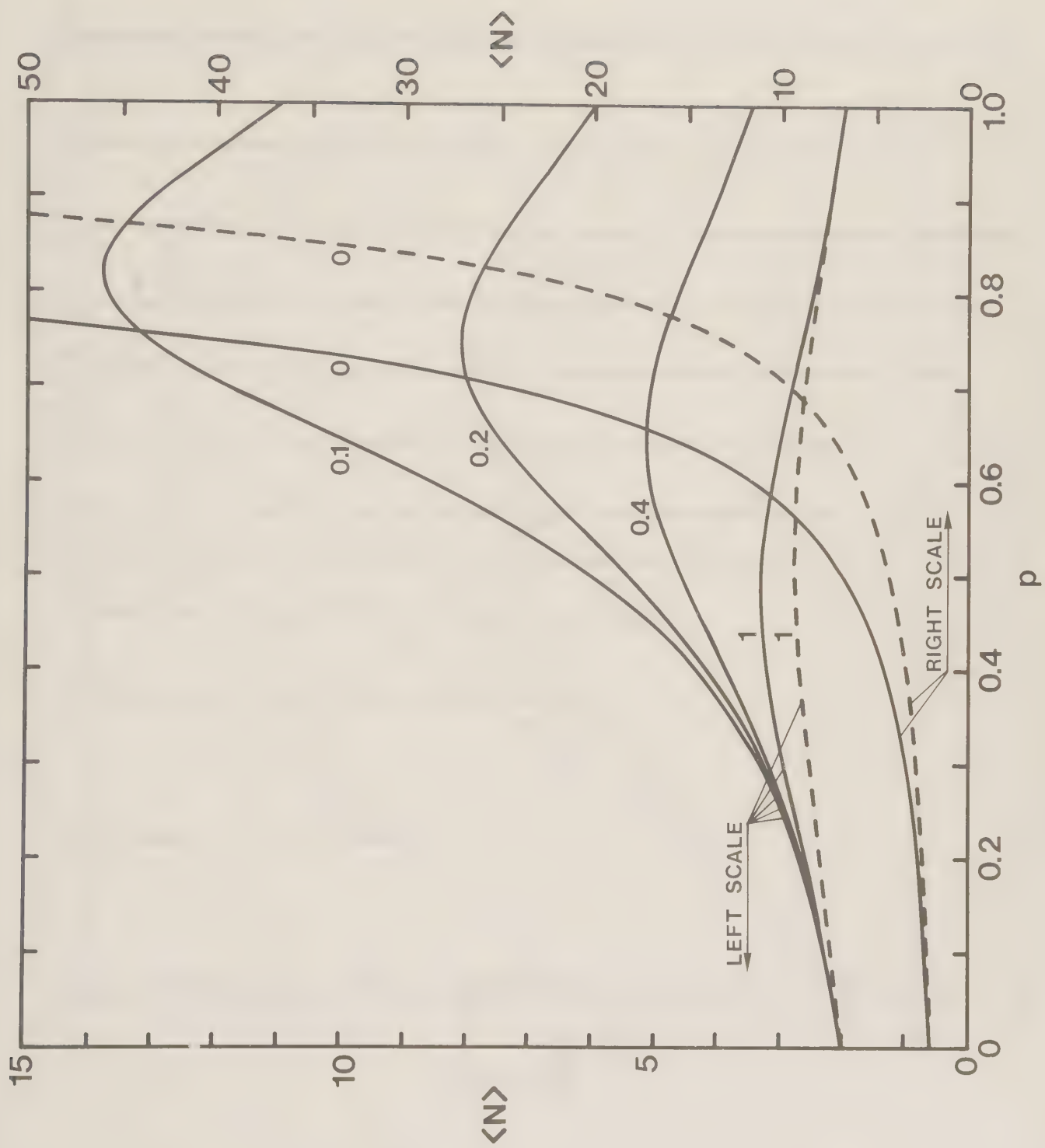


FIG. 8



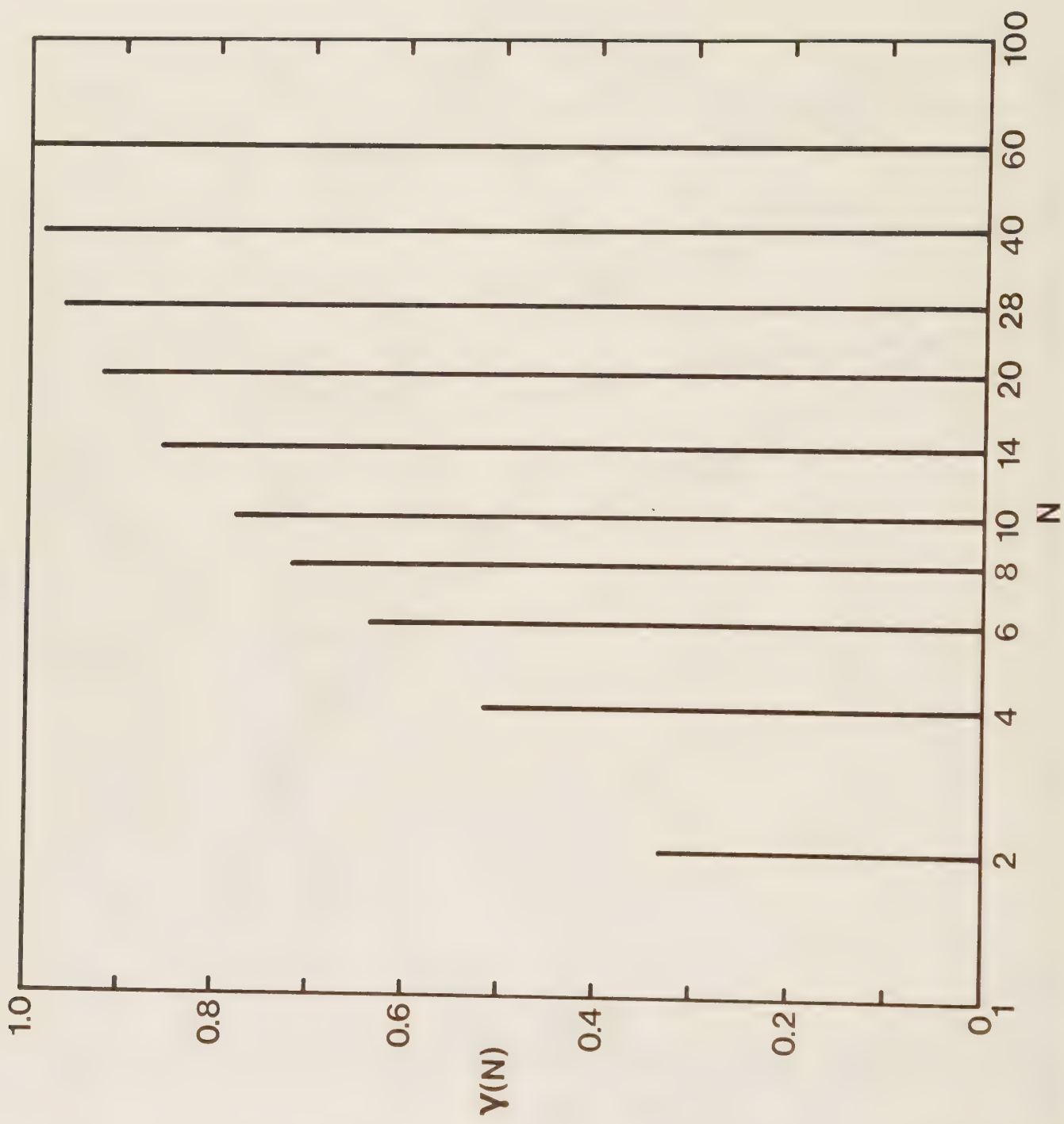
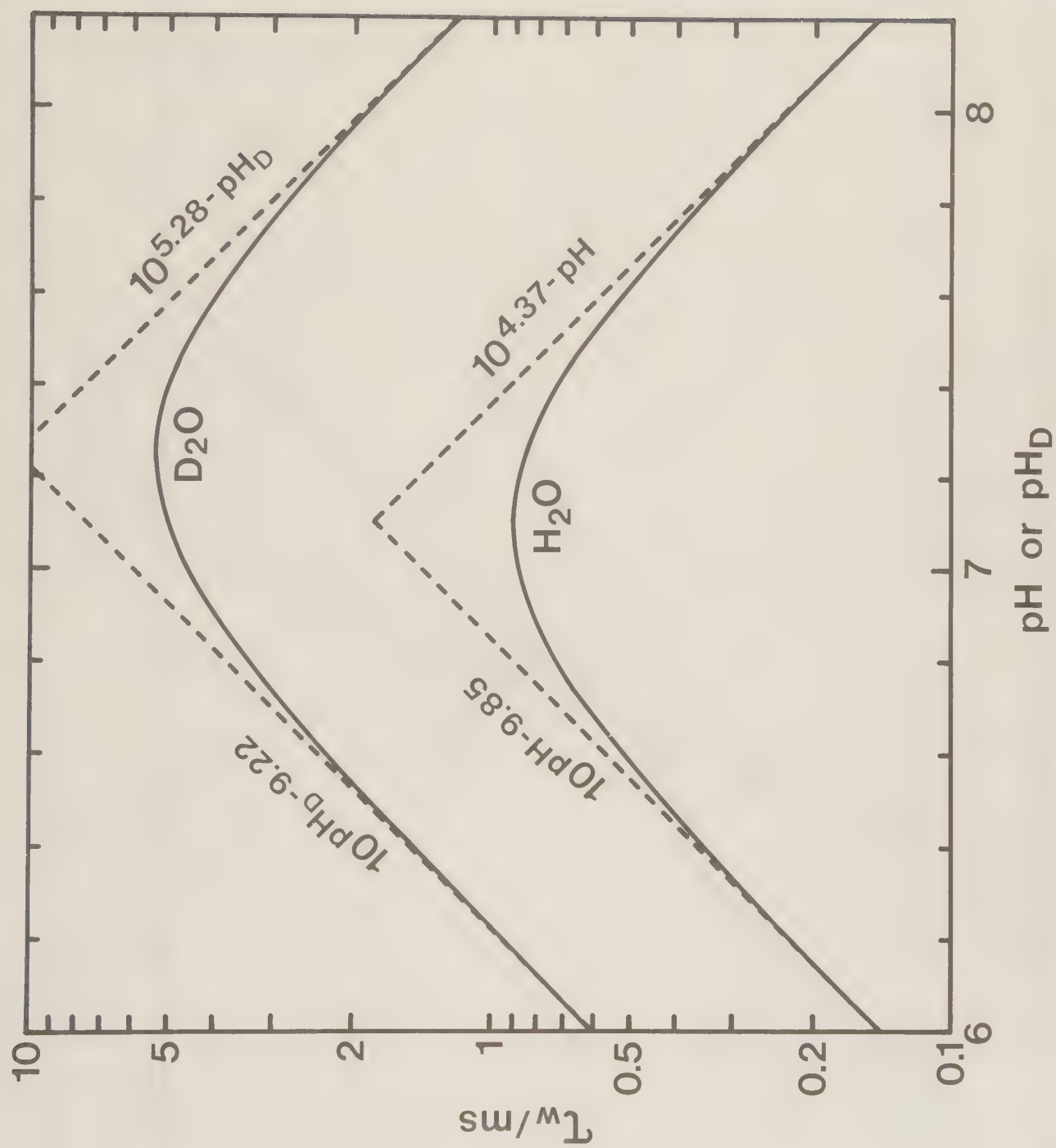


FIG. 10



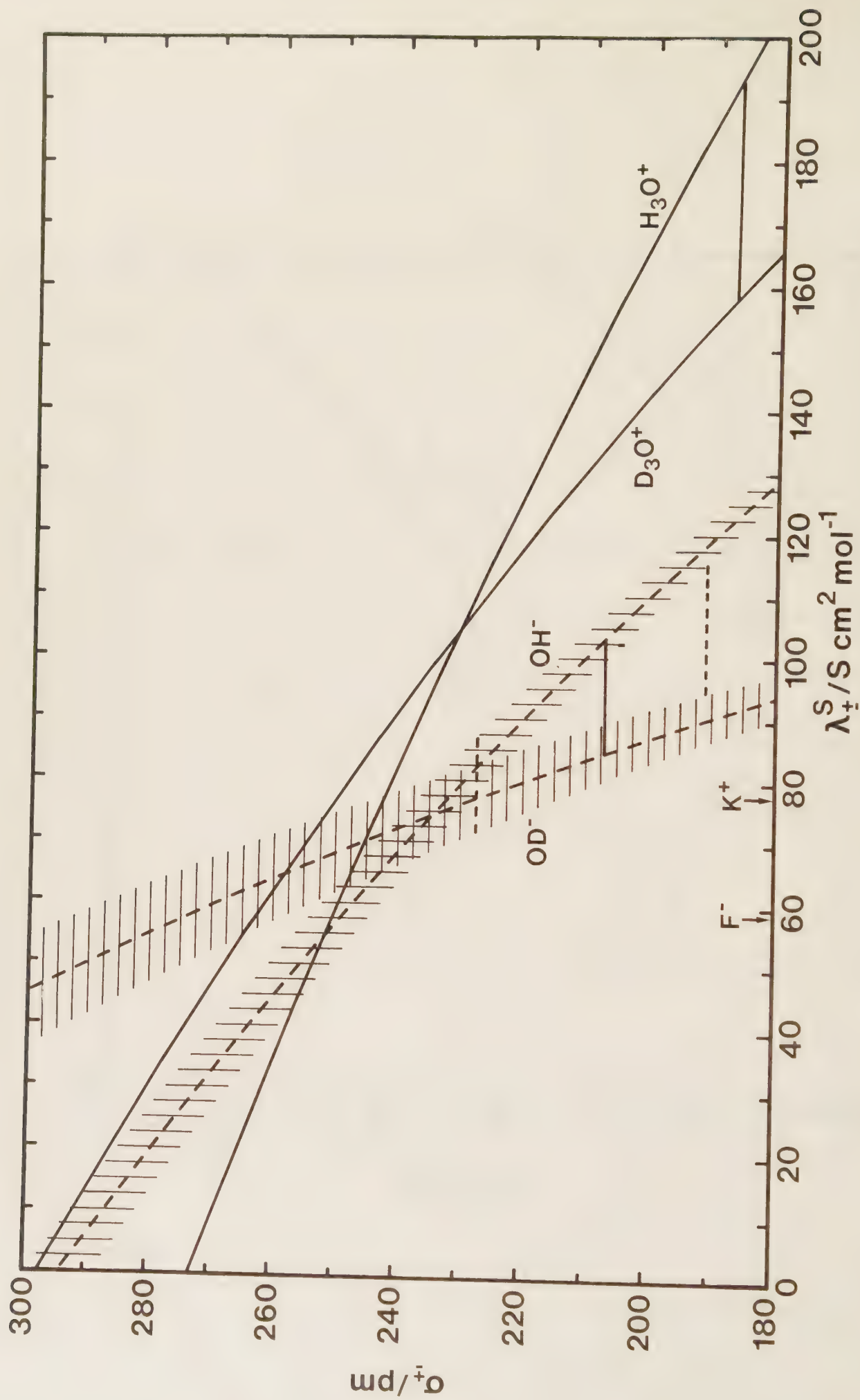
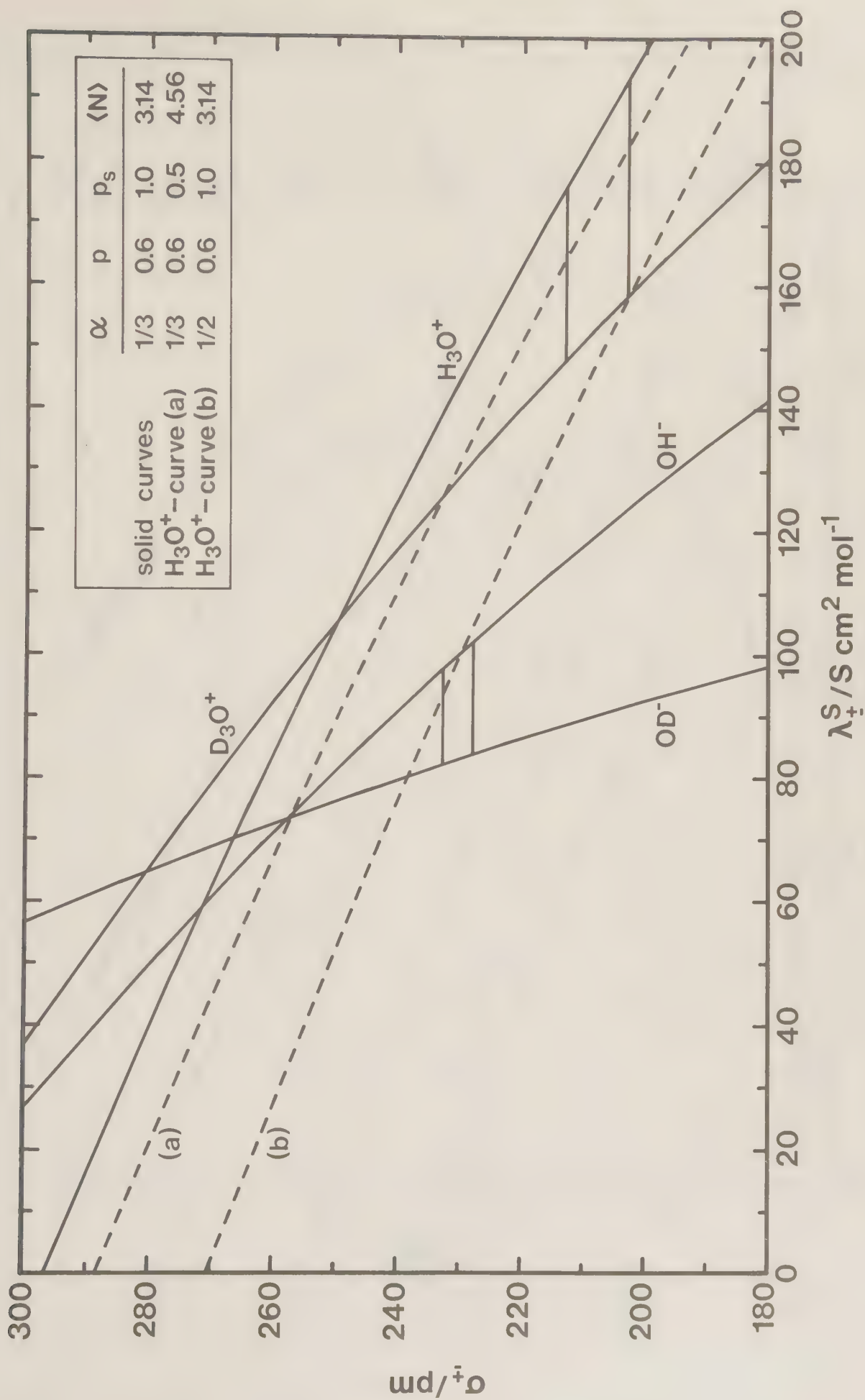


FIG. 12



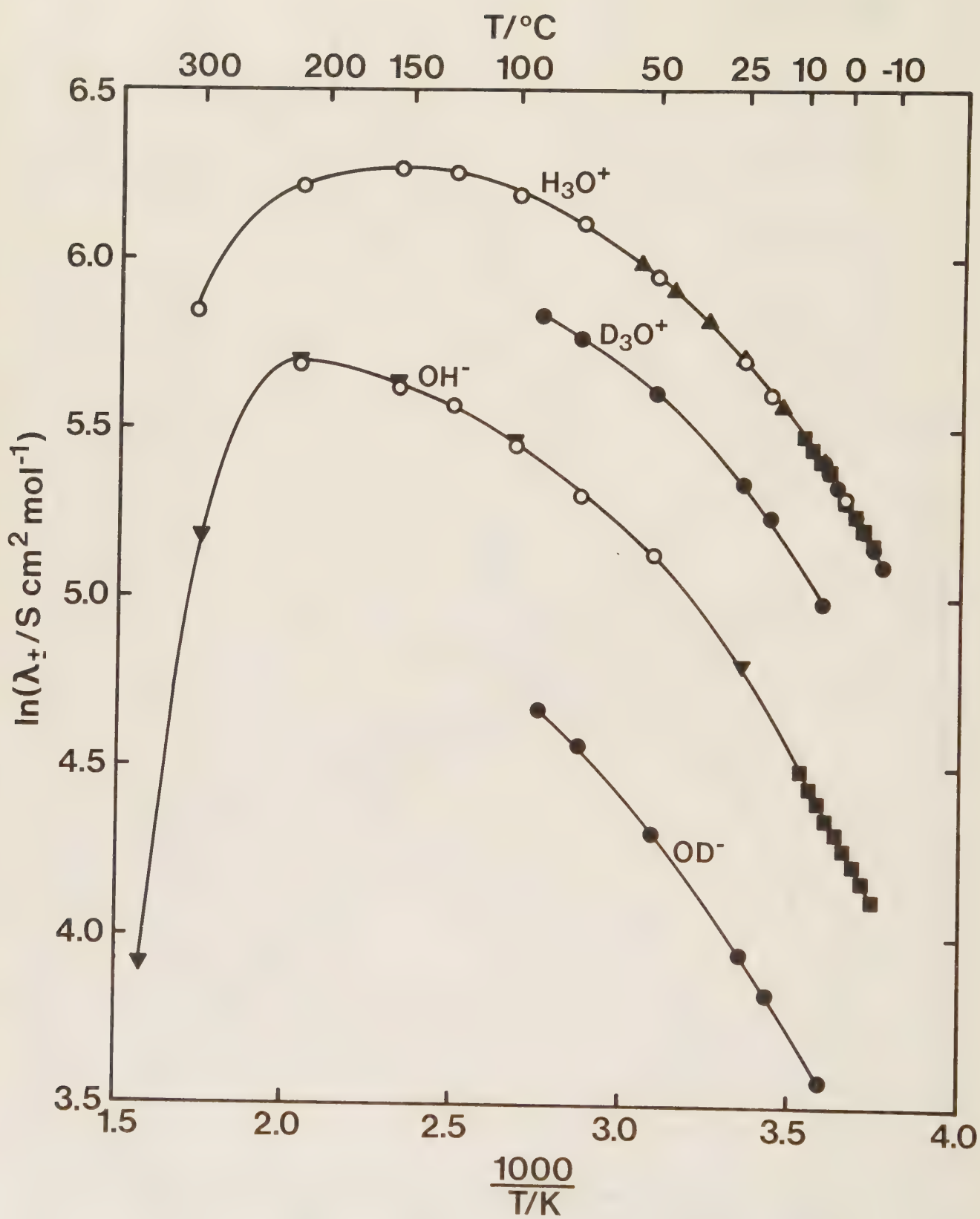


FIG. 14

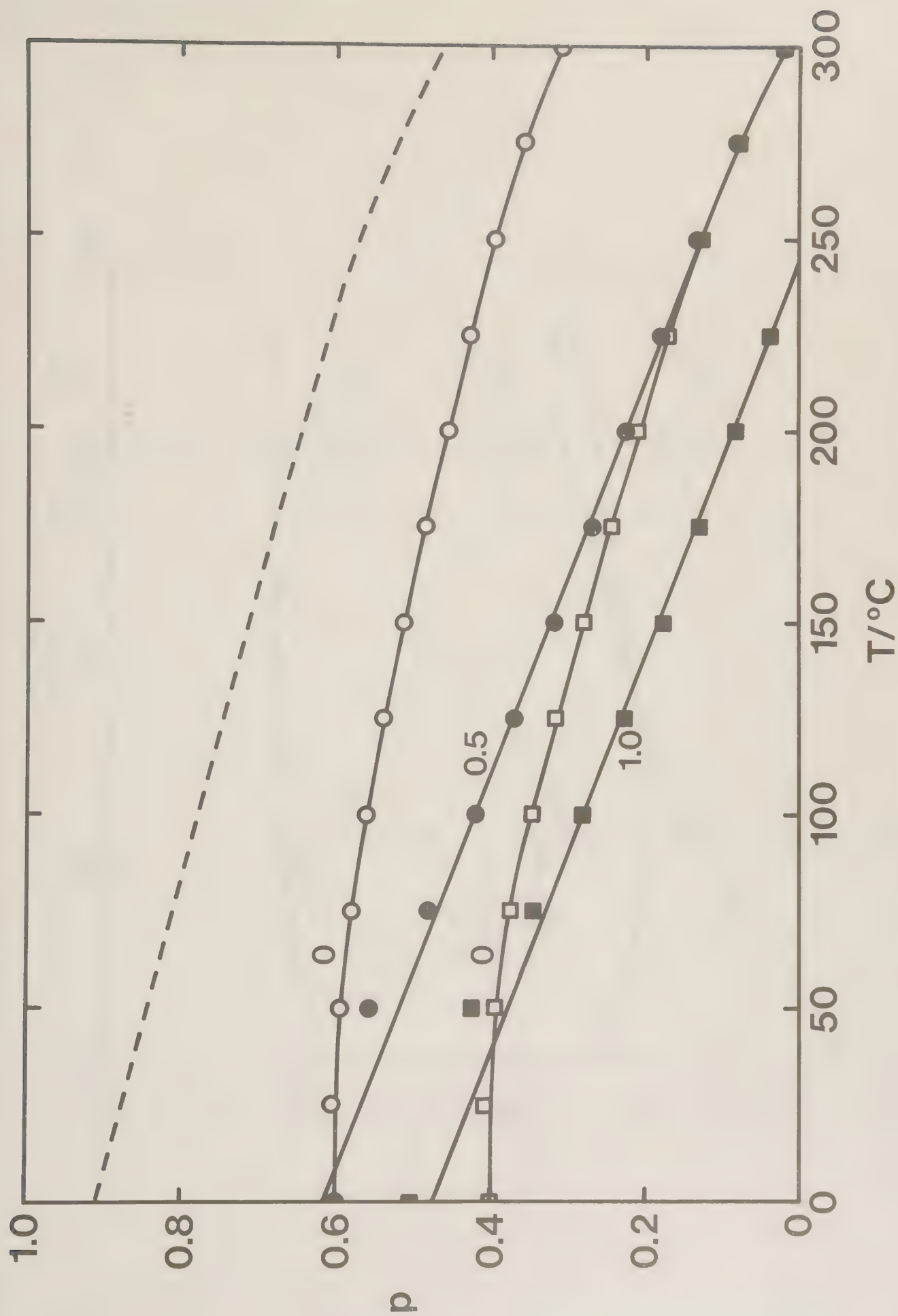


FIG. 15

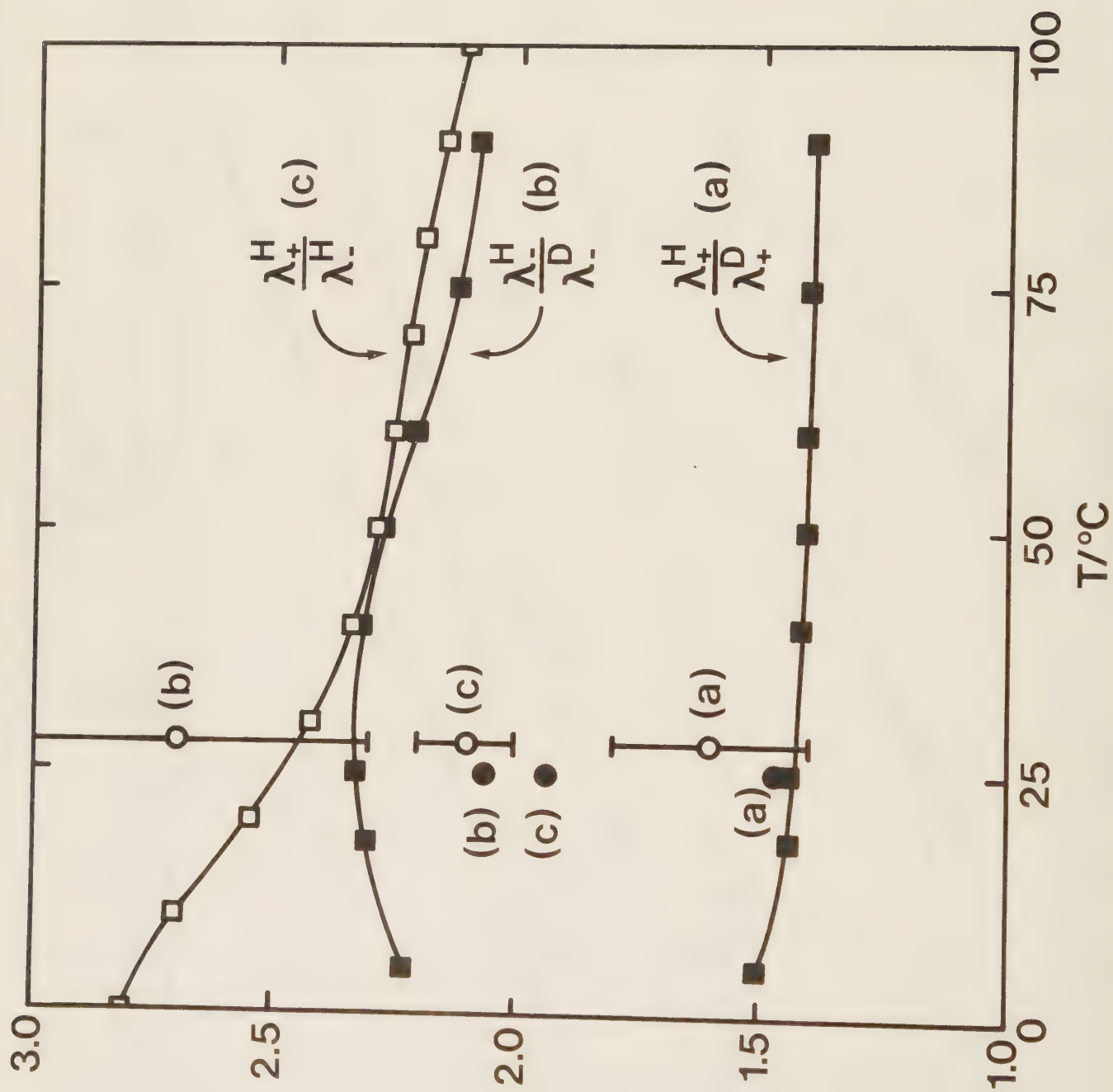


FIG. 16

